STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 121692

TO: Zohreh Fay
Location: 4a59 / 4c70
Monday, May 17, 2004
Art Unit: 1614
Phone: 272-0573
Serial Number: 09 / 445919

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes

121692

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

RECEIVED
MAY 10 2004
STIC

Requester's Full Name: Zohreh Fay Examiner #: 66646 Date: 5/10/04
Art Unit: 1614 Phone Number 308-(571)272-0573 Serial Number: 09/445,919
Mail Box and Bldg/Room Location: 4C70 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: See Bib sheet

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

please search the claimed composition and use, specifically the composition of claims 1 and 2 and the use of claims 9 and 10.

Jan

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Jan	NA Sequence (#) _____	STN ✓
Searcher Phone #: 22504	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) ✓	Questel/Orbit _____
Date Searcher Picked Up: 5/17/04	Bibliographic _____	Dr.Link _____
Date Completed: 5/17/04	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: 20	Patent Family _____	WWW/Internet _____
Online Time: + 120	Other _____	Other (specify) _____

PTO-1590 (8-01)

=> fil reg
FILE 'REGISTRY' ENTERED AT 15:34:18 ON 17 MAY 2004

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 MAY 2004 HIGHEST RN 682330-24-1
DICTIONARY FILE UPDATES: 16 MAY 2004 HIGHEST RN 682330-24-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

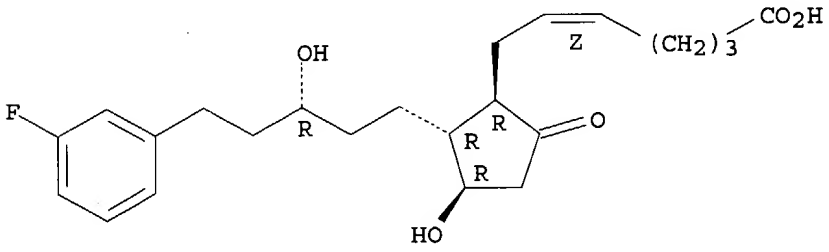
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide can tot l29

L29 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **219828-15-6** REGISTRY
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(3R)-5-(3-fluorophenyl)-3-hydroxypentyl]-3-hydroxy-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H31 F O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

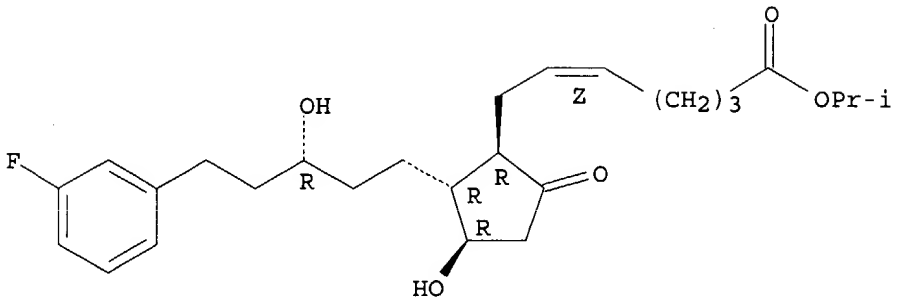
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:119579

L29 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **219827-63-1** REGISTRY
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(3R)-5-(3-fluorophenyl)-3-hydroxypentyl]-3-hydroxy-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH

MF C26 H37 F O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.

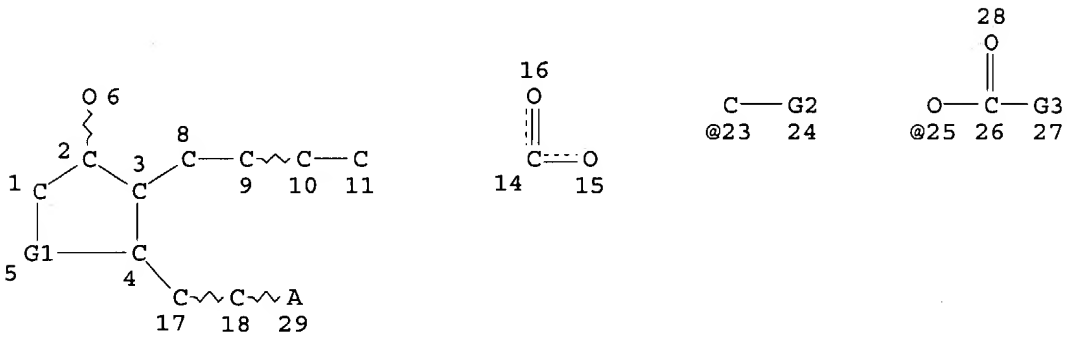


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:119579

=> d sta que l74
L72 STR



VAR G1=C/23
VAR G2=OH/ME/ET/OME/25
VAR G3=AK/CY
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 11
CONNECT IS E3 RC AT 14
CONNECT IS M1 RC AT 15
CONNECT IS M1 RC AT 29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 4
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L74 10918 SEA FILE=REGISTRY CSS FUL L72

100.0% PROCESSED 34389 ITERATIONS 10918 ANSWERS
SEARCH TIME: 00.00.02

=> d his

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               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 13:49:29 ON 17 MAY 2004
L1             1 S WO98-SE1368/AP,PRN OR SE97-2706/AP,PRN
               E STJERNSCHANTZ J/AU
L2            85 S E3-E7
               E RESUL B/AU
L3            50 S E3,E4
               E LAKE S/AU
L4            34 S E3-E7,E13
               SEL RN L1

     FILE 'REGISTRY' ENTERED AT 13:50:50 ON 17 MAY 2004
L5            38 S E1-E38
L6            11 S L5 AND 46.150.18/RID AND F/ELS AND NR>=2
L7             6 S L6 NOT SI/ELS
L8            27 S L5 NOT L6
L9            22 S L8 AND NR>=1
L10           18 S L9 NOT SI/ELS
L11           12 S L10 NOT 46.150.18/RID
L12            4 S L11 NOT C4/ES
L13            2 S L12 AND C5/ES
               E PGE2/CN
L14            1 S E3

     FILE 'HCAPLUS' ENTERED AT 13:59:52 ON 17 MAY 2004
L15          139 S L2-L4 NOT L1

     FILE 'REGISTRY' ENTERED AT 14:00:04 ON 17 MAY 2004

     FILE 'HCAPLUS' ENTERED AT 14:00:04 ON 17 MAY 2004
               SET SMARTSELECT ON
L16          SEL L15 1- RN :     782 TERMS
               SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 14:00:10 ON 17 MAY 2004
L17          782 S L16
L18          176 S L17 AND C5/ES
L19           48 S L18 AND 1/NR
L20            5 S L19 AND PGE2
L21            6 S L17 AND TRINOR
L22            6 S L18 AND DIHYDRO
L23          814 S L5,L17
L24           21 S L23 AND 46.150.18/RID AND F/ELS
L25           13 S L24 NOT (N OR SI)/ELS
L26           11 S L25 AND NR>=2
L27            9 S L26 NOT S/ELS
L28            8 S L27 NOT C15H13FO2
               SEL RN 1 6
L29            2 S E1-E2
L30           61 S L23 AND 15
L31           55 S L30 NOT C6/ES
L32           50 S L31 NOT UNSPECIFIED
L33           39 S L32 NOT (SI OR N OR S)/ELS
L34           13 S L33 NOT 16.127.1/RID
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L35          26 S L33 NOT L34
L36           3 S L35 AND "E2"
L37          23 S L35 NOT L36
L38           2 S L37 AND PGE2
L39          21 S L37 NOT L38
L40           2 S L39 AND C20H32O5

     FILE 'HCAPLUS' ENTERED AT 14:20:46 ON 17 MAY 2004
L41        7491 S TRIMETHYLENE
L42           3 S L41 AND PGE2
L43          23 S L41 AND ?PROSTA?
L44           4 S L43 AND "E2"
L45          19 S L43 NOT L44
L46           4 S L45 AND 16 16

     FILE 'REGISTRY' ENTERED AT 14:24:26 ON 17 MAY 2004
L47           1 S 63357-23-3
L48          51 S L23 AND C5/ES AND 1/NR
L49          10 S L48 NOT 16.127.1/RID
L50          41 S L48 NOT L49
L51          29 S L50 NOT (SI OR S OR N)/ELS
L52          23 S L51 AND (15S OR 15R)
L53           6 S L51 NOT L52
L54          13 S L52 AND OXO
L55          10 S L52 NOT L54
               E PGE2
L56         211 S E3
L57         198 S L56 AND 15
L58          51 S L56 AND 15R
L59         126 S L56 AND 15S
L60         198 S L57-L59
L61         154 S L60 AND 1/NR
L62         141 S L61 NOT (N OR S OR SI OR P)/ELS
L63          73 S L62 NOT ESTER
L64          70 S L63 NOT L23
L65          66 S L64 AND 1/NC
L66          21 S L65 AND 16
L67           7 S L66 AND 16 16
L68          16 S L62 AND 16 16
L69           9 S L68 NOT L67
L70             STR
L71          50 S L70 CSS
L72             STR L70
L73          50 S L72 CSS SAM
L74       10918 S L72 CSS FUL

     FILE 'HCAPLUS' ENTERED AT 15:22:13 ON 17 MAY 2004
L75           1 S L29
               E PROSTANOID RECEPTOR/CT
L76         271 S E7
L77           9 S L76 AND ?GLAUCOM?
L78           8 S L76 AND (EYE OR ?OCULAR?)(L)(?HYPERTENS? OR ?HYPOTENS?)
               E GLAUCOMA/CT
L79         110 S E3
L80        3766 S E4-E6
               E E4+ALL
L81        3876 S E9,E10,E8+NT
L82         723 S E12-E13/BI
               E E14+ALL
L83        1362 S E3
L84           8 S L76 AND L79-L83
L85       42287 S L74
L86         198 S L76 AND L85
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L87          10 S L75,L77,L78,L84
L88           6 S L86 AND L87
L89          10 S L87,L88
L90         473 S L85 AND EP1
L91           7 S L90 AND L79-L83
L92           8 S L90 AND ?GLAUCOM?
L93          11 S L90 AND (EYE OR ?OCULAR?)(L)(?HYPERTENS? OR ?HYPOTENS?)
L94          16 S L89,L91-L93
L95           1 S L2-L4 AND L75
L96          51 S L2-L4 AND L85
L97           2 S L96 AND EP1
L98          22 S L96 AND L79-L83
L99          26 S L96 AND ?GLAUCOM?
L100         12 S L96 AND (EYE OR ?OCULAR?)(L)(?HYPERTENS? OR ?HYPOTENS?)
L101         16 S L1,L94,L95,L97
L102         49 S L96,L98-L100 NOT L101
L103         35 S L102 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L104          8 S L101 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L105          3 S L104 AND PGE2
L106          8 S L104,L105
L107          7 S L106 NOT 3/SC
L108          8 S L101 NOT L106
L109          1 S L108 AND RESUL ?/AU
L110          8 S L107,L109
L111         12 S L103 AND (PGE2 OR "E2")
                SEL DN AN 11 12 L111
L112          2 S E1-E6 AND L111
L113         10 S L110,L112

     FILE 'REGISTRY' ENTERED AT 15:34:18 ON 17 MAY 2004

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:34:37 ON 17 MAY 2004
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FILE COVERS 1907 - 17 May 2004  VOL 140 ISS 21
FILE LAST UPDATED: 16 May 2004  (20040516/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

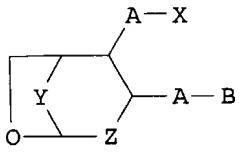

=> => d all hitstr tot l113

L113 ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:770134  HCAPLUS
DN   137:279023
ED   Entered STN:  10 Oct 2002
TI   Preparation of thromboxane ligands without blood clotting side effects
IN   Burk, Robert M.; Krauss, Achim H. P.; Woodward, David F.
```

PA Allergan, Inc., USA
SO U.S., 18 pp., Cont.-in-part of U.S. Ser. No. 331,356, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D307-93
ICS A01K031-343
NCL 514469000
CC 26-3 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63
FAN.CNT 6

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 6462077	B1	20021008		US 2001-899713	20010705	<--
	US 5416106	A	19950516		US 1993-174534	19931228	<--
	US 5516791	A	19960514		US 1995-378414	19950126	<--
	US 5650431	A	19970722		US 1996-645467	19960513	<--
	US 5741812	A	19980421		US 1997-832431	19970402	<--
	US 2003109571	A1	20030612		US 2002-213190	20020805	<--
PRAI	US 1993-174534	A3	19931228	<--			
	US 1995-378414	A2	19950126	<--			
	US 1996-645467	A2	19960513	<--			
	US 1997-832431	A1	19970402	<--			
	US 1998-38068	B1	19980311	<--			
	US 1999-331356	B2	19990616				
	US 1999-334356	B2	19990616				
	US 2001-899713	A1	20010705				

OS MARPAT 137:279023
GI



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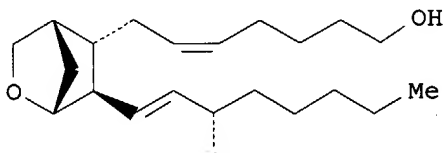


II

AB Thromboxane agonists of formula I [A = alkylene, alkenylene, etc.; B = Me, cycloalkyl, aryl, heteroaryl, etc.; X = (substituted) CH2OH, (substituted) CO2H, etc.; Y = (CH2)n; n = 1-2; Z = (CH2)m; m = 0-1] are prepared The compds. are used for the treatment of **ocular hypotension**, **hypertension**, hemorrhage, myocardial ischemia, angina pectoris, coronary contraction, cerebrovascular contraction after subarachnoidal hemorrhage, cerebral hemorrhage and asthma. Thus, II was prepared from U-46619 in two steps. II exhibited pronounced activity in contracting vascular smooth muscle.

ST thromboxane ligand prepn **ocular hypotension**; hemorrhage treatment thromboxane agonist prepn

IT Thromboxanes
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(agonists; preparation of thromboxane ligands without blood clotting side effects)

IT Heart, disease
(angina pectoris; preparation of thromboxane ligands without blood clotting side effects)

IT Thromboxanes
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(antagonists; preparation of thromboxane ligands without blood clotting side effects)

IT Meninges
(disease, subarachnoid hemorrhage; preparation of thromboxane ligands without blood clotting side effects)

IT Brain, disease
(hemorrhage; preparation of thromboxane ligands without blood clotting side effects)

IT Heart, disease
(ischemia; preparation of thromboxane ligands without blood clotting side effects)

IT **Hypotension**
(**ocular**; preparation of thromboxane ligands without blood clotting side effects)

IT Cell aggregation
(platelet; preparation of thromboxane ligands without blood clotting side effects)

IT Asthma
Cardiac contraction
Hemorrhage
Human
Hypertension
(preparation of thromboxane ligands without blood clotting side effects)

IT Thromboxane receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of thromboxane ligands without blood clotting side effects)

IT Hypertension
(pulmonary; preparation of thromboxane ligands without blood clotting side effects)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP; preparation of thromboxane ligands without blood clotting side effects)

IT **Prostanoid receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type **EP1**; preparation of thromboxane ligands without blood clotting side effects)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP3; preparation of thromboxane ligands without blood clotting side effects)

IT 167270-44-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of thromboxane ligands without blood clotting side effects)

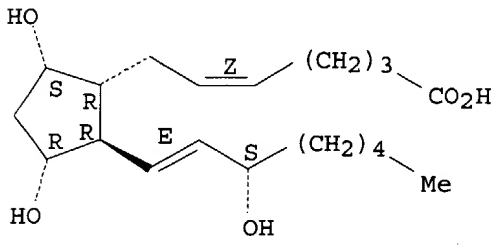
IT 159359-94-1P 159359-95-2P 159359-97-4P 159359-98-5P 167270-49-7P
167270-51-1P 193149-59-6P 193149-60-9P 193149-61-0P 193149-62-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thromboxane ligands without blood clotting side effects)

IT 75-31-0, Isopropylamine, reactions **551-11-1**, PGF2α
3282-30-2, Trimethylacetyl chloride 56985-40-1, U-46619
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thromboxane ligands without blood clotting side effects)

IT **65147-38-8P 71845-64-2P 135877-48-4P**
136198-86-2P 147555-69-9P **147555-72-4P** 159359-93-0P
159359-96-3P 167270-42-0P 167270-43-1P 167270-45-3P 167270-46-4P
167270-47-5P 167270-48-6P 304854-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

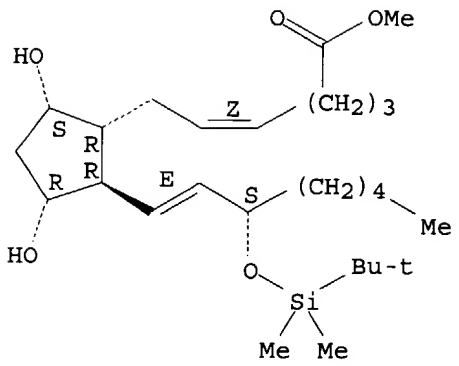
(preparation of thromboxane ligands without blood clotting side effects)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; EP 0364417 1990 HCAPLUS
(2) Bito; US 4599353 A 1986 HCAPLUS
(3) Bito, L; Applied Pharmacology in the Medical Treatment of Glaucomas 1984, P477 HCAPLUS
(4) Bito, L; Arch Ophthalmol 1987, V105, P1036 MEDLINE
(5) Burk; US 5416106 A 1995 HCAPLUS
(6) Burk; US 5516791 A 1996 HCAPLUS
(7) Burk; US 5741812 A 1998 HCAPLUS
(8) Burk; Tetrahedron Letters 1993, V34(3), P395 HCAPLUS
(9) Chan; US 4994274 A 1991 HCAPLUS
(10) Chan; US 5034413 A 1991 HCAPLUS
(11) Coleman, R; Br J Pharmacol V73, P773 HCAPLUS
(12) Grover; US 4931460 A 1990 HCAPLUS
(13) Larock; US 4436934 A 1984 HCAPLUS
(14) Lieb; US 4622339 A 1986 HCAPLUS
(15) Nilsson; Invest Ophtalmol Vis Sci 1987, suppl, P284
(16) Siebold; Prodrug 1989, V5, P3
(17) Starr, M; Exp Eye Research 1971, P170 HCAPLUS
IT **551-11-1**, PGF2α
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thromboxane ligands without blood clotting side effects)
RN 551-11-1 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



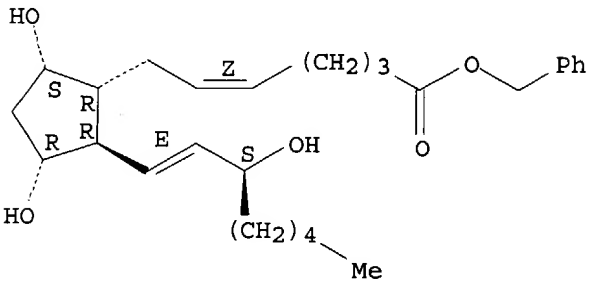
IT **65147-38-8P 71845-64-2P 135877-48-4P**
136198-86-2P 147555-72-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thromboxane ligands without blood clotting side effects)
RN 65147-38-8 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 15-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11-dihydroxy-, methyl ester, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



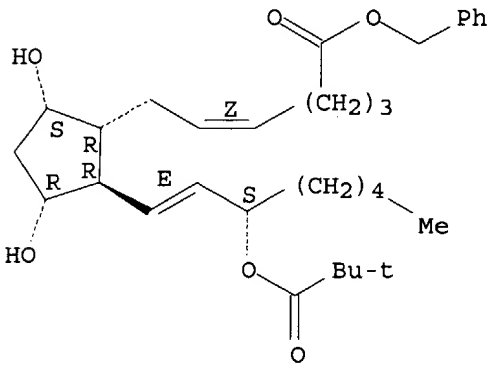
RN 71845-64-2 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, phenylmethyl ester, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 135877-48-4 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, phenylmethyl ester, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

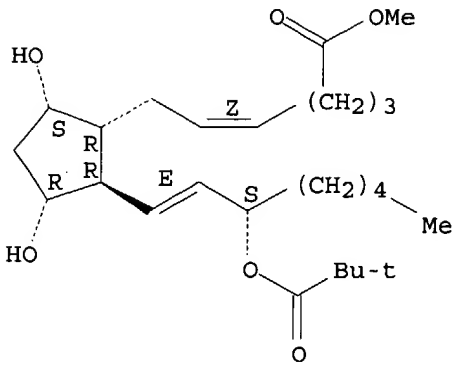
Absolute stereochemistry.
Double bond geometry as shown.



RN 136198-86-2 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, methyl ester, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

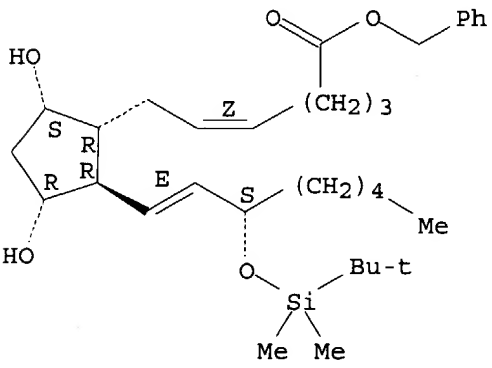
Absolute stereochemistry.

Double bond geometry as shown.



RN 147555-72-4 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 15-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11-dihydroxy-, phenylmethyl ester, (5Z,9α,11α,13E,15S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L113 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:404486 HCAPLUS
DN 133:275770
ED Entered STN: 20 Jun 2000
TI Microvascular effects of selective prostaglandin analogues in the eye with special reference to latanoprost and **glaucoma** treatment
AU **Stjernschantz, Johan**; Selen, Goran; Astin, Maria; **Resul, Bahram**
CS Department of Neuroscience, Unit of Pharmacology, Uppsala University, Uppsala, Swed.
SO Progress in Retinal and Eye Research (2000), 19(4), 459-496
CODEN: PRTRES; ISSN: 1350-9462
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
Section cross-reference(s): 2
AB A review with many refs. Prostaglandin F2α analogs have recently been introduced on the market for **glaucoma** treatment. While these drugs have a well-documented intraocular pressure reducing effect only a limited number of studies have been published regarding their effects on the microvasculature in the eye. Since many naturally occurring

prostaglandins have marked effects on the cardiovascular system it is conceivable that synthetic prostaglandins used as **glaucoma** drugs may exert microvascular effects in the eye, even if they exhibit receptor selectivity. Latanoprost, the active principle of Xalatan eye drops, is a selective FP prostanoid receptor agonist, and much of the paper is focused on the microvascular effects of latanoprost and some closely related prostaglandin analogs. The purpose of the paper is to review the literature on the microvascular effects of prostaglandins in the eye, and to present some unpublished data on the effects of selective prostaglandin analogs. Most of the prostaglandin analogs studied exhibit selectivity for the FP prostanoid receptor. Results from studies with the following prostaglandin analogs are presented in the paper: PGF2α-iso-Pr ester (PGF2α-IE), 17-phenyl-18,19,20-trinor-PGF2α-iso-Pr ester (17-phenyl-PGF2α-IE), 15-keto-17-phenyl-18,19,20-trinor-PGF2α-iso-Pr ester (15-keto-17-phenyl-PGF2α-IE), 13,14-dihydro-17-phenyl-18,19,20-trinor-PGF2α-iso-Pr ester (latanoprost), 13,14-dihydro-15R,S-17-phenyl-18,19,20-trinor-PGF2α-iso-Pr ester (PhXA34), 17-phenyl-18,19,20-trinor-PGE2-iso-Pr ester (17-phenyl-PGE2-IE), and 19R-hydroxy-PGE2 (19R-OH-PGE2). The regional blood flow has been determined with radioactively labeled microspheres, the blood volume with 51Cr labeled erythrocytes and the capillary permeability to albumin with 125I and 131I labeled albumin. PGF2α-IE has been shown to exert marked microvascular effects in the rabbit anterior segment including vasodilation, increased capillary permeability, and a breakdown of the blood-aqueous barrier. 17-Phenyl-PGF2α-IE, 15-keto-17-phenyl-PGF2α-IE, and PhXA34/latanoprost exerted significantly less vasodilatory effect, and little effect on capillary permeability was seen with the FP receptor agonists when studied with Evans blue. I.v. administration of PhXA34 at a dose range of 1-100 μg/kg b.w. had no consistent effect on the regional blood flow in the eye indicating that FP receptors in the ocular blood vessels are not expressed in the rabbit, or alternatively are not functionally coupled to regulation of vascular tone. In cats topical application of PGF2α-IE had no significant effect the on the regional blood flow in cannulated eyes. No blood flow expts. were performed in intact eyes with PGF2α-IE, 17-phenyl-PGF2α-IE and latanoprost caused some vasodilation in the anterior segment. None of the analogs had any significant effect on the blood volume in the ocular tissues, but an increase in capillary permeability to albumin was seen in several tissues of the eye. However, in the eyelid, nictitating membrane and conjunctiva exposed to high concns. of the prostaglandins no or only little leakage of albumin was detected. It appears that the intraocular microvasculature in the cat exhibits some sensitivity to FP prostanoid receptor agonists. In the cynomolgus monkey eye PGF2α-IE has been shown to cause a dramatic increase in blood flow of the anterior uvea, but only weak effect was detected with the selective FP receptor agonists and an **EP1** receptor agonist after topical administration. I.v. infusion of latanoprost at a dose range of 0.6-6 μg/kg b.w. had little effect on the blood flow in most ocular tissues, and the same was true for 17-phenyl-PGE2, a relatively selective **EP1** receptor agonist, after intracardiac infusion at about the same dose range. I.v. infusion of the EP2 receptor agonist 19R-OH-PGE2 markedly reduced the vascular resistance in the eye. No significant effect was seen on the blood volume in the ocular tissues with any of the FP receptor agonists after topical administration. PGF2α-IE increased the capillary permeability to albumin in the anterior segment and possibly the retina, but 17-phenyl-PGF2α-IE and latanoprost/PhXA34 had no effect on capillary permeability in any of the ocular tissues. Based on the results of previous studies and the expts. described in the present paper it is evident that PGF2α has significant microvascular effects in the rabbit, cat and monkey eye, causing vasodilation and/or increased capillary permeability, whereas selective FP receptor agonists such as latanoprost exert no or minimal effects in the primate eye, and markedly reduced microvascular effects in the rabbit eye. However, little

difference between PGF2α and the selective FP receptor agonists was seen in the cat eyes. It also appears that the **EP1** receptor like the FP receptor is not involved in the regulation of vascular tone in the primate eye, whereas stimulation of the EP2 receptor reduces the vascular resistance in the monkey eye. Finally, the microvascular parameters in the control eyes of cats and monkeys are compared and discussed.

ST review prostaglandin analog latanoprost **antiglaucoma** microvascular effect; species difference eye vascular tone latanoprost **antiglaucoma** review

IT Capillary vessel
(endothelium; microvascular effects of prostaglandins in the eye)

IT **Antiglaucoma agents**
Eye
Species differences
(microvascular effects of prostaglandins in the eye)

IT Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(microvascular effects of prostaglandins in the eye)

IT Circulation
(regional; microvascular effects of prostaglandins in the eye)

IT **130209-82-4**, Latanoprost
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(microvascular effects of prostaglandins in the eye)

RE.CNT 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Abran, D; Circulation Res 1997, V80, P463 HCAPLUS
(2) Alm, A; Acta Physiol Scand 1972, V84, P306 MEDLINE
(3) Alm, A; Adler's Physiology of the Eye 1987, P182
(4) Alm, A; Bibliotheca Anatomica 1977, V16, P24
(5) Alm, A; Exp Eye Res 1973, V15, P15 MEDLINE
(6) Alm, A; Ophthalmology 1995, V102, P1743 MEDLINE
(7) Alm, A; Prog Retinal Eye Res 1998, V17, P291 HCAPLUS
(8) Alm, A; Surv Ophthalmol 1997, V41(Suppl 2), PS105
(9) Alm, A; The Ocular Effects of Prostaglandins and Other Eicosanoids 1989, P447 HCAPLUS
(10) Anggard, E; Acta Physiol Scand 1971, V81, P396 HCAPLUS
(11) Anggard, E; Europ J Pharmacol 1971, V14, P66 HCAPLUS
(12) Anggard, E; Therapeutic Applications of Prostaglandins 1993, P1
(13) Astin, M; Compr Summ Uppsala Dissertations Faculty of Medicine 1998, V179
(14) Astin, M; Europ J Pharmacol 1997, V340, P195 HCAPLUS
(15) Astin, M; Exp Eye Res 1994, V59, P401 HCAPLUS
(16) Astin, M; J Ocular Pharmacol Therapeutics 1998, V14, P119 HCAPLUS
(17) Basu, S; Prostaglandins Leukot Essent Fatty Acids 1994, V50, P161 HCAPLUS
(18) Basu, S; Prostaglandins Leukot Essent Fatty Acids 1997, V57, P305 HCAPLUS
(19) Benezra, D; Am J Ophthalmol 1978, V86, P455 HCAPLUS
(20) Bill, A; Acta Physiol Scand 1964, V60, P18 MEDLINE
(21) Bill, A; Acta Physiol Scand 1968, V73, P204 HCAPLUS
(22) Bill, A; Acta Physiol Scand 1979, V105, P437 HCAPLUS
(23) Bill, A; Acta Physiol Scand 1980, V108, P419 HCAPLUS
(24) Bito, L; Comp Biochem Physiol 1972, V42A, P65
(25) Bito, L; Exp Eye Res 1973, V16, P299 HCAPLUS
(26) Bito, L; Exp Eye Res 1987, V44, P217 HCAPLUS
(27) Bito, L; J Physiol 1972, V221, P371 HCAPLUS
(28) Bito, L; Surg Ophthalmol 1997, V41(Suppl 2), PS1
(29) Bjork, J; Adv Tromboxane Leukotriene Res 1983, V12, P1 HCAPLUS
(30) Camber, O; Int J Pharmaceutics 1986, V29, P259 HCAPLUS
(31) Camber, O; Int J Pharmaceutics 1987, V37, P27 HCAPLUS
(32) Camras, C; Curr Eye Res 1981, V1, P205 HCAPLUS
(33) Camras, C; Invest Ophthalmol Vis Sci 1977, V16(Suppl), P57
(34) Camras, C; Invest Ophthalmol Vis Sci 1987, V28, P463 HCAPLUS
(35) Camras, C; Ophthalmology 1996, V103, P138 MEDLINE
(36) Chemtob, S; Invest Ophthalmol Vis Sci 1991, V32, P1799 MEDLINE

(37) Cheng-Bennett, A; Invest Ophthalmol Vis Sci 1990, V21, P1389
(38) Coleman, R; Comprehensive Medicinal Chemistry 1989, V3, P634
(39) Coleman, R; Pharmacol Rev 1994, V46, P205 HCAPLUS
(40) Cooper, C; Arch Ophthalmol 1980, V98, P1102 MEDLINE
(41) Crawford, K; Curr Eye Res 1987, V6, P1035 HCAPLUS
(42) Denton, J; J Neurosur 1972, V36, P34
(43) Deutsch, T; Am J Ophthalmol 1979, V87, P537
(44) Eakins, K; Br J Med 1972, V19, P452
(45) Eakins, K; Exp Eye Res 1974, V19, P141 HCAPLUS
(46) Eakins, K; Exp Eye Res 1977, V25(Suppl), P483
(47) Frucht, J; Br J Ophthalmol 1984, V68, P656 MEDLINE
(48) Gabelt, B; Exp Eye Res 1989, V49, P389 HCAPLUS
(49) Ginderdeuren, R; Invest Ophthalmol Vis Sci 1992, V33, P3378
(50) Goh, Y; Biochim Biophys Acta 1987, V921, P302 MEDLINE
(51) Green, K; Arch Ophthalmol 1985, V103, P569 HCAPLUS
(52) Habib, A; J Biol Chem 1997, V272, P7191 HCAPLUS
(53) Hanss, J; Therapeutic Applications of Prostaglandins 1993, P37
(54) Hardy, P; Inv Ophthalmol Vis Sci 1994, V35, P580 MEDLINE
(55) Haugen, C; Scand J Lab Invest 1992, V52, P141
(56) Hickam, J; Invest Ophthalmol 1965, V4, P876 MEDLINE
(57) Hirata, M; Nature 1991, V349, P617 HCAPLUS
(58) Hoste, A; Ophthalmology 1997, V104, P895 MEDLINE
(59) Hoyng, P; Surv Ophthalmol 1997, V41(Suppl 2), PS83
(60) Jampol, L; Ophthalmology 1982, V89, P891 MEDLINE
(61) Jampol, L; Ophthalmology 1985, V92, P807 MEDLINE
(62) Jonsson, H; Science 1975, V187, P1093 HCAPLUS
(63) Kawai, Y; Am J Physiol 1991, V260, PH1538 HCAPLUS
(64) Kelly, R; Nature 1976, V260, P544 HCAPLUS
(65) Lippton, H; Prostaglandins Biology and Chemistry of Prostaglandins and Related Eicosanoids 1988, P217
(66) Miyake, K; Archives of Ophthalmology 1999, V117(1), P34 HCAPLUS
(67) Miyake, K; Br J Ophthalmol 1980, V64, P324 MEDLINE
(68) Miyake, K; Graefe's Arch Clin Exp Ophthalmol 1977, V203, P81 MEDLINE
(69) Miyake, K; Jpn J Ophthamol 1978, V22, P80
(70) Miyake, K; The Ocular Effects of Prostaglandins and Other Eicosanoids 1989, P265 HCAPLUS
(71) Namba, T; Nature 1993, V365, P166 HCAPLUS
(72) Narumiya, S; Physiol Rev 1999, V79, P1193 HCAPLUS
(73) Nicolela, M; Am J Ophthalmol 1996, V122, P784 HCAPLUS
(74) Nielsen, P; Exp Eye Res 1989, V48, P329 HCAPLUS
(75) Nilsson, S; Exp Eye Res 1989, V48, P707 HCAPLUS
(76) Ocklind, A; Invest Ophthalmol Vis Sci 1996, V37, P716 MEDLINE
(77) Ohkubo, B; Curr Eye Res 1987, V6, P1197
(78) Pace-Asciak, C; Prostaglandins Biology and Chemistry of Prostaglandins and Related Eicosanoids 1988, P46
(79) Pennick, M; J Neurol 1972, V37, P398
(80) Peyman, G; Ann Ophthalmol 1975, V7, P279 HCAPLUS
(81) Pickard, J; Nature 1973, V245, P187 HCAPLUS
(82) Pierce, K; J Biol Chem 1997, V272, P883 HCAPLUS
(83) Pierce, K; Trends Pharmacol Sci 1995, V16, P253 HCAPLUS
(84) Pournaras, C; Exp Eye Res 1978, V26, P687 HCAPLUS
(85) Pournaras, C; Ocular Blood Flow Glaucoma-Meeting 1995, P40
(86) Resul, B; Curr Opin Ther Patents 1993, V3, P781
(87) Resul, B; J Med Chem 1993, V36, P243 HCAPLUS
(88) Rochels, R; Doc Ophthalmol 1984, V57, P215 MEDLINE
(89) Rowe, J; Am J Ophthalmol 1997, V124, P683 MEDLINE
(90) Sakurai, M; Jpn J Ophthalmol 1991, V35, P156 HCAPLUS
(91) Sakurai, M; Jpn J Ophthalmol 1993, V37, P252 HCAPLUS
(92) Schuster, V; Surv Ophthalmol 1997, V41(Suppl 2), PS41
(93) Seong, G; Ophthalmologica 1999, V213, P355 HCAPLUS
(94) Sjoquist, B; Arzneim-Forsch/Drug Res 1999, V49, P234 MEDLINE
(95) Sjoquist, B; Arzneim-Forsch/Drug Res 1999, V49, P240 MEDLINE
(96) Sjoquist, B; Drug Metabolism and Disposition 1998, V26, P745 HCAPLUS

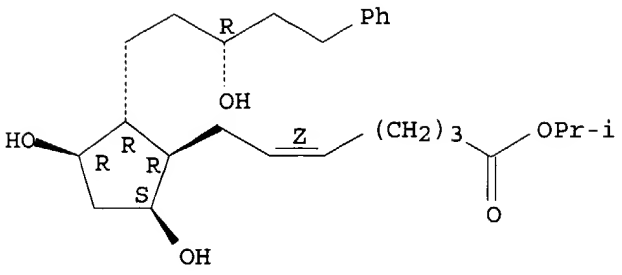
(97) Starr, M; Exp Eye Res 1971, V11, P161 HCAPLUS
(98) Starr, M; Exp Eye Res 1971, V11, P170 HCAPLUS
(99) Stjernschantz, J; Advances in Prostaglandin, Thromboxane and Leukotriene Research 1995, V23, P513 HCAPLUS
(100) Stjernschantz, J; Arch Ophthalmol 1999, V117, P1363 HCAPLUS
(101) Stjernschantz, J; Curr Opin Ophthamol 1996, V7, P11 MEDLINE
(102) Stjernschantz, J; Drugs Future 1992, V17, P691
(103) Stjernschantz, J; Handbook of Experimental Pharmacology 1984, V69, P311 HCAPLUS
(104) Stjernschantz, J; Prostaglandins 1984, V27, P5 HCAPLUS
(105) Stjernschantz, J; The Ocular Effects of Prostaglandins and Other Eicosanoids 1989, P155 HCAPLUS
(106) Stjernschantz, J; Uveoscleral Outflow Biology and Clinical Aspects 1998, P57
(107) Su, E; Invest Ophthalmol Vis Sci 1994, V35, P998 MEDLINE
(108) Sugimoto, Y; J Biol Chem 1993, V268, P2712 HCAPLUS
(109) Sugiyama, T; Jpn J Ophthalmol 1995, V39, P124 HCAPLUS
(110) Taniguchi, T; J Ocul Pharmacol 1996, V12, P489 HCAPLUS
(111) Taylor, P; Nature 1974, V250, P665 HCAPLUS
(112) Toris, C; Ophthalmology 1993, V100, P1297 MEDLINE
(113) Unger, W; The Ocular Effects of Prostaglandins and Other Eicosanoids 1989, P293 HCAPLUS
(114) Ushikubi, F; J Biol Chem 1989, V264, P16496 HCAPLUS
(115) Uski, T; Acta Physiol Scand 1984, V120, P197 HCAPLUS
(116) Uski, T; Acta Physiol Scand 1984, V121, P369 HCAPLUS
(117) Vane, J; Improved Non-Steroid Anti-Inflammatory Drugs: COX-2 Enzyme Inhibitors 1996, P1
(118) Villumsen, J; Br J Ophthalmol 1989, V73, P419 MEDLINE
(119) Warwar, R; Ophthalmology 1998, V105, P263 MEDLINE
(120) Watson, P; Ophthalmology 1996, V103, P126 MEDLINE
(121) Wendling, W; Stroke 1991, V22, P66 HCAPLUS
(122) Whitelock, R; Arch Ophthalmol 1973, V89, P495
(123) Wistrand, P; Surv Ophthalmol 1997, V41(Suppl 2), PS129
(124) Woodward, D; Ophthalmic Res 1985, V17, P318 HCAPLUS
(125) Woodward, D; Prostaglandins 1993, V46, P371 HCAPLUS
(126) Woodward, D; Surv Ophthalmol 1997, V41(Suppl 2), PS15
(127) Yamamoto, T; J Glaucoma 1997, V6, P430 MEDLINE
(128) Yamamoto, T; Surv Ophthalmol 1997, V41(Suppl 2), PS99
(129) Ziche, M; Advances in Prostaglandin, Thromboxane and Leukotriene Research 1995, V23, P495 HCAPLUS
(130) Ziche, M; Int J Cancer 1985, V35, P549 HCAPLUS
(131) Ziche, M; J Nat Cancer Inst 1982, V69, P475 HCAPLUS

IT **130209-82-4**, Latanoprost
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(microvascular effects of prostaglandins in the eye)

RN 130209-82-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L113 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:344852 HCAPLUS
DN 131:5147
ED Entered STN: 07 Jun 1999
TI Preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivatives for use as **ocular hypertensive** agents
IN Burk, Robert M.
PA Allergan Sales, Inc., USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-557
ICS C07D277-30
CC 26-3 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63
FAN.CNT 3

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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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	US 1996-740883	A3	19961104	<--		
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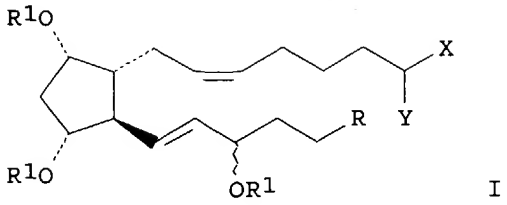
GI



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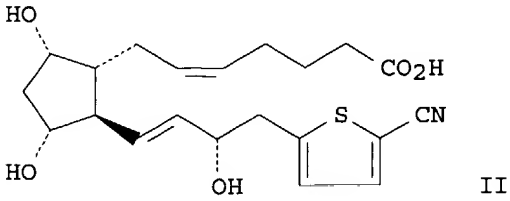


II

AB F-type prostaglandins I [R = heteroaryl such as thienyl; R1 = H, alkyl; X = OH, alkyloxy; Y = :O, H2] were prepared and formulated for use as **ocular hypertensive** agents. Thus, thienylprostaglandin II was prepared starting from [4-(2,5-dichloro-3-thienyl)-2-oxobutyl]-phosphonic acid di-Me ester and (3aα,4α,5β,6aα)-hexahydro-2-oxo-5-[(tetrahydro-2H-pyran-2-yl)oxy]-2H-cyclopenta[b]furan-4-carboxaldehyde. The prepared compds. were tested for binding activity to various prostanoid receptors, including **EP1**, EP2, and EP3.

ST prostaglandin **ocular hypertensive** prepn; prostanoid receptor binding prostaglandin prepn

IT Prostanoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(EP2; preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

IT Prostanoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(EP3; preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

IT Prostaglandins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(F-type; preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

IT Prostanoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

IT **225660-96-8P 225660-97-9P 225660-98-0P 225660-99-1P 225661-00-7P 225661-65-4P 225661-66-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

IT **185067-61-2P** 225661-01-8P 225661-02-9P 225661-03-0P 225661-04-1P 225661-05-2P 225661-06-3P 225661-07-4P 225661-08-5P 225661-09-6P **225661-10-9P 225661-11-0P 225661-12-1P 225661-13-2P 225661-14-3P**

225661-15-4P 225661-16-5P **225661-17-6P** 225661-19-8P
225661-22-3P 225661-24-5P 225661-27-8P
225661-30-3P 225661-32-5P 225661-34-7P
225661-36-9P **225661-39-2P** 225661-41-6P 225661-43-8P
225661-44-9P 225661-46-1P 225661-48-3P
225661-50-7P **225661-51-8P 225661-52-9P** 225661-54-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

IT 75-04-7, Ethylamine, reactions 75-30-9, 2-Iodopropane 141-43-5, 2-Hydroxyethylamine, reactions 17814-85-6 143393-77-5 185067-71-4 185068-04-6 225661-67-6 225661-69-8 225661-70-1 225661-71-2
225661-75-6 225661-77-8 225661-79-0
225661-82-5 225661-83-6 **225661-84-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

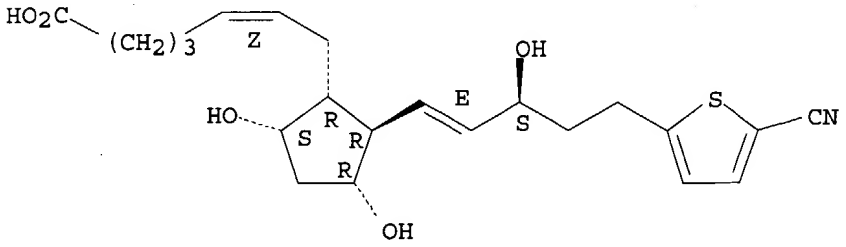
IT 225661-55-2P 225661-56-3P **225661-57-4P** 225661-59-6P
225661-60-9P 225661-61-0P 225661-62-1P 225661-63-2P
225661-64-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Allergan Inc; WO 9636599 A 1996 HCAPLUS
(2) Allergan Inc; WO 9731895 A 1997 HCAPLUS
(3) Burk, R; US 5834498 A 1998 HCAPLUS

IT **225660-96-8P 225660-97-9P 225660-98-0P**
225660-99-1P 225661-00-7P 225661-65-4P
225661-66-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

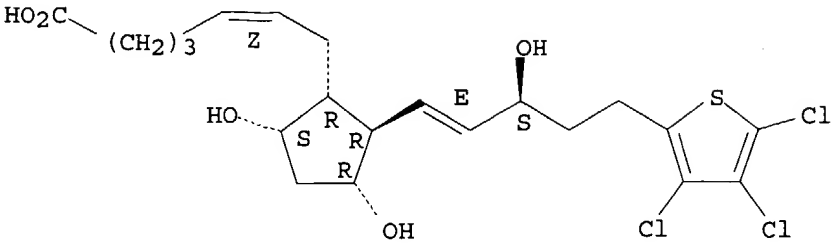
RN 225660-96-8 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-cyano-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



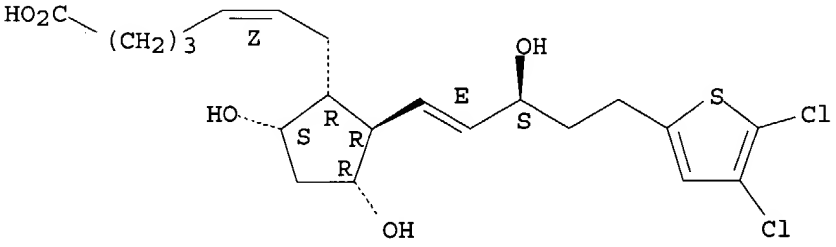
RN 225660-97-9 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3,4,5-trichloro-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



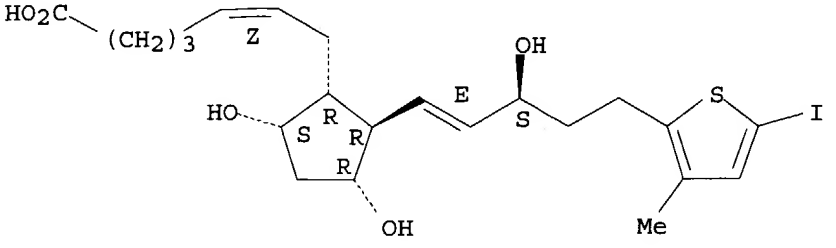
RN 225660-98-0 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4,5-dichloro-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



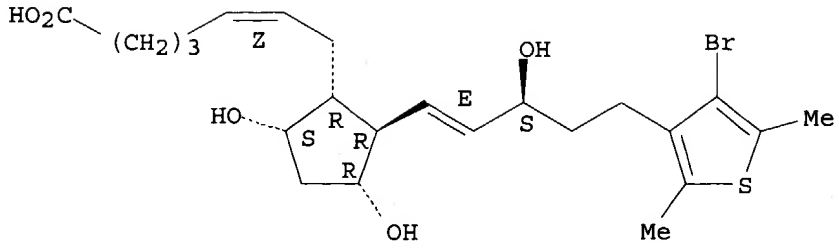
RN 225660-99-1 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(5-iodo-3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



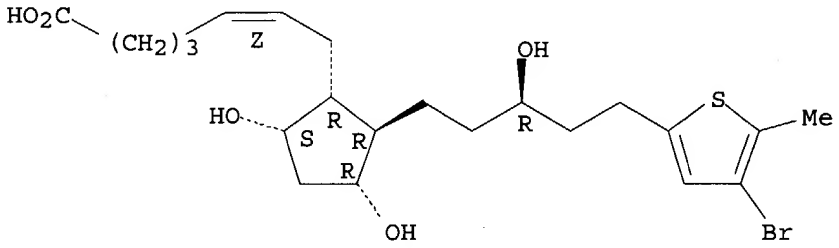
RN 225661-00-7 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-2,5-dimethyl-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



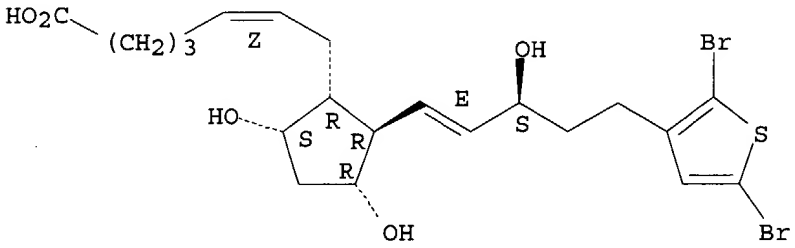
RN 225661-65-4 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(3R)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxypentyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 225661-66-5 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(2,5-dibromo-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

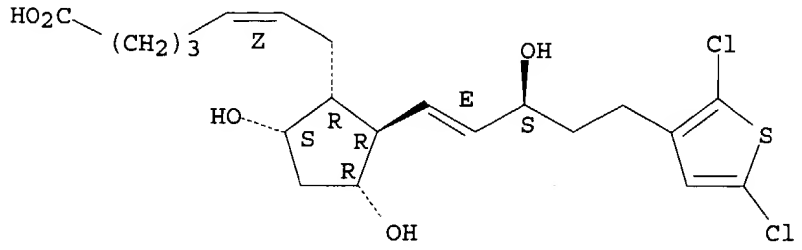
Relative stereochemistry.
Double bond geometry as shown.



IT **185067-61-2P 225661-10-9P 225661-11-0P**
225661-12-1P 225661-13-2P 225661-14-3P
225661-15-4P 225661-17-6P 225661-22-3P
225661-24-5P 225661-27-8P 225661-30-3P
225661-32-5P 225661-34-7P 225661-39-2P
225661-44-9P 225661-46-1P 225661-48-3P
225661-51-8P 225661-52-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)
RN 185067-61-2 HCAPLUS

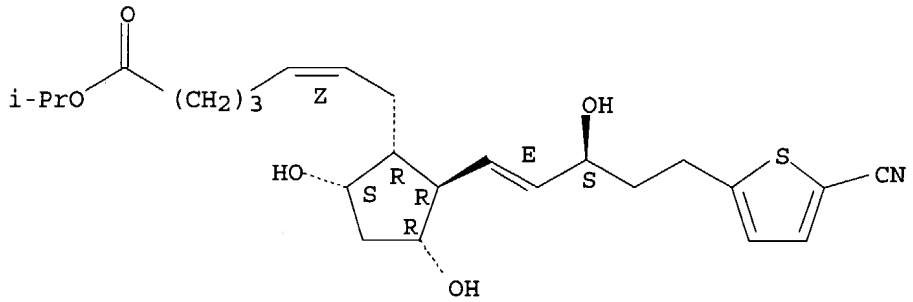
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(2,5-dichloro-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



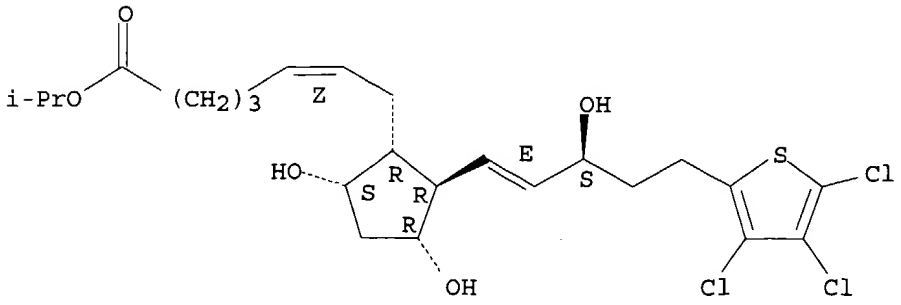
RN 225661-10-9 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-cyano-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 225661-11-0 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3,4,5-trichloro-2-thienyl)-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

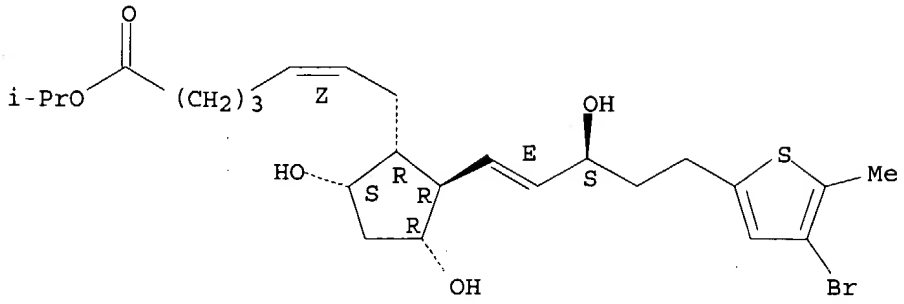
Relative stereochemistry.
Double bond geometry as shown.



RN 225661-12-1 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, 1-methylethyl

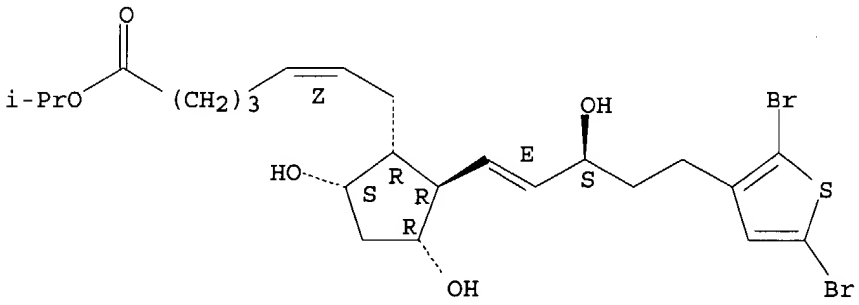
ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



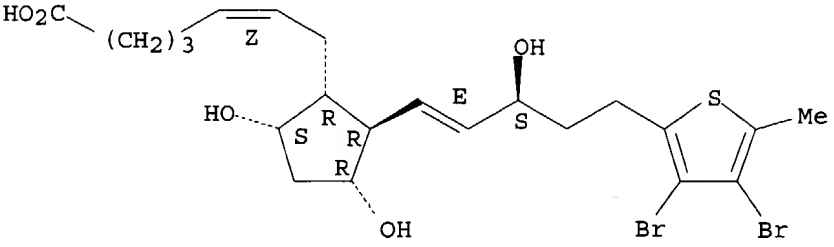
RN 225661-13-2 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(2,5-dibromo-3-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



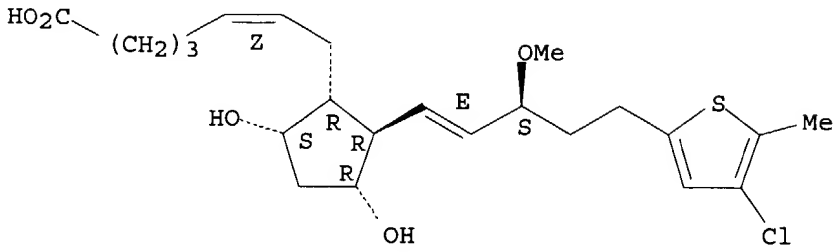
RN 225661-14-3 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



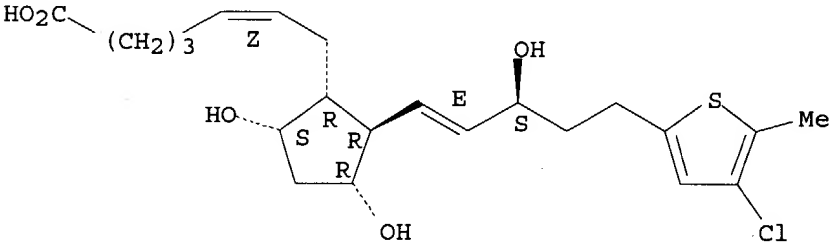
RN 225661-15-4 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-chloro-5-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



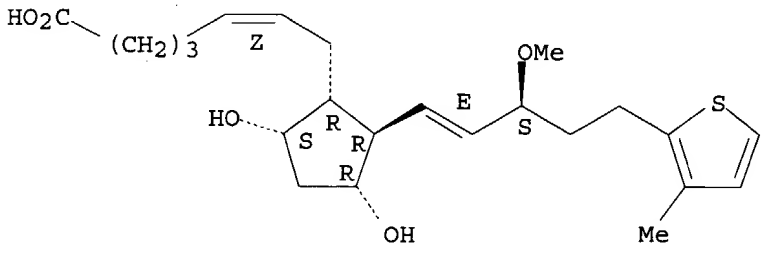
RN 225661-17-6 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-chloro-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



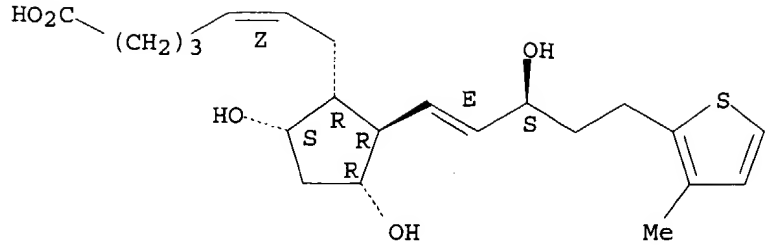
RN 225661-22-3 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-methoxy-5-(3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



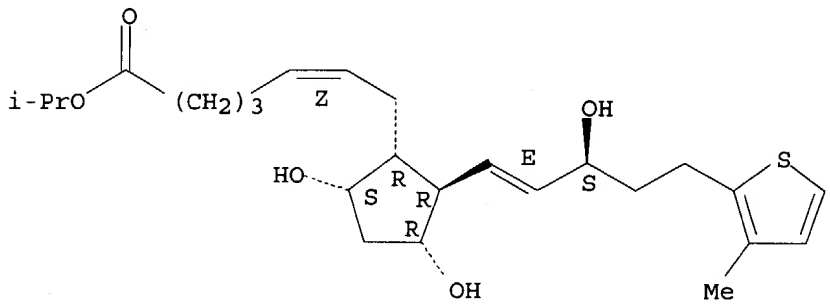
RN 225661-24-5 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



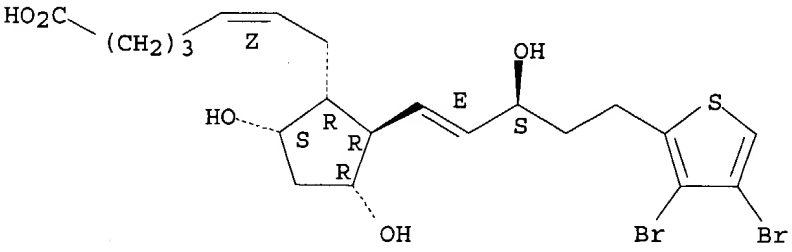
RN 225661-27-8 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5R)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



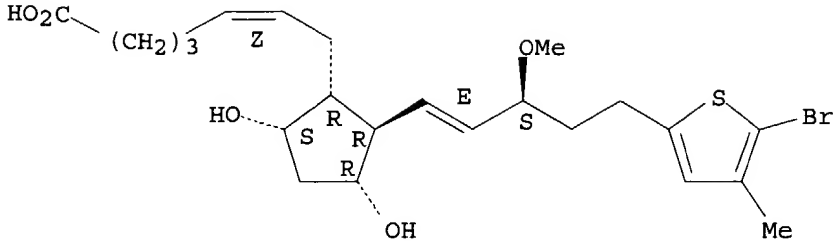
RN 225661-30-3 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



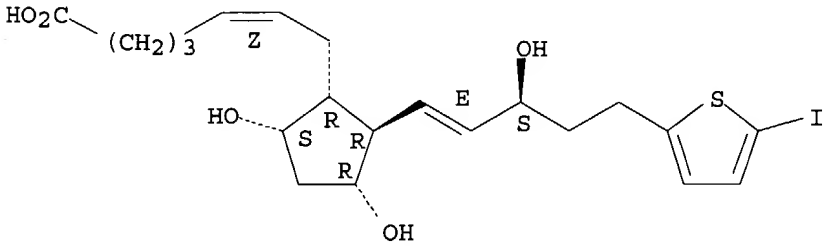
RN 225661-32-5 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-bromo-4-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



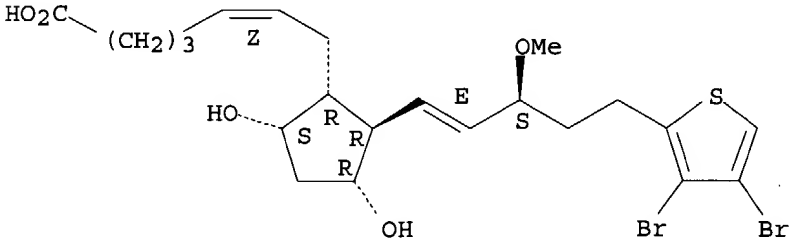
RN 225661-34-7 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(5-iodo-2-thienyl)-1-pentenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



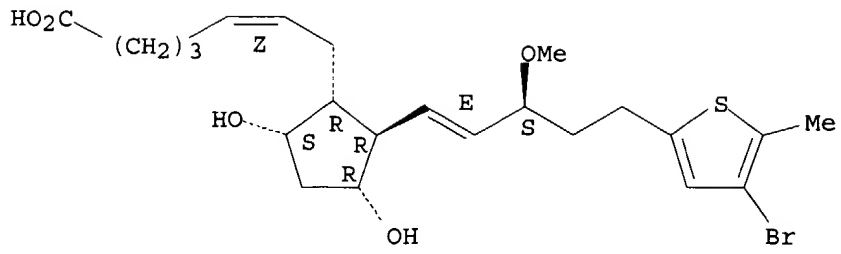
RN 225661-39-2 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



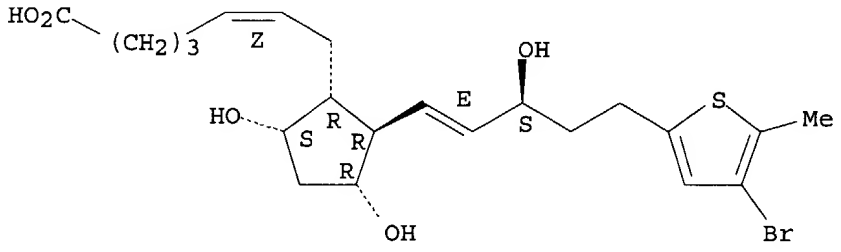
RN 225661-44-9 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



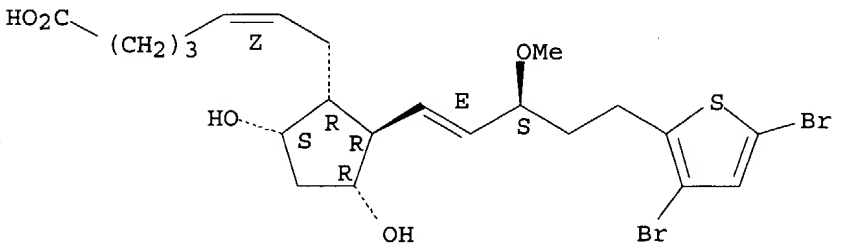
RN 225661-46-1 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



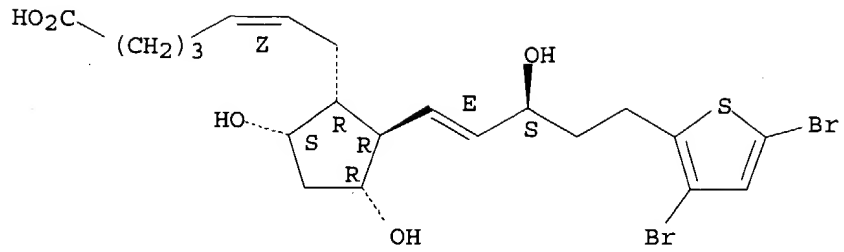
RN 225661-48-3 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,5-dibromo-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



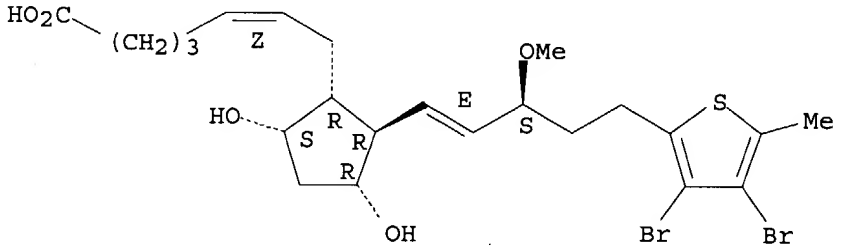
RN 225661-51-8 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,5-dibromo-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



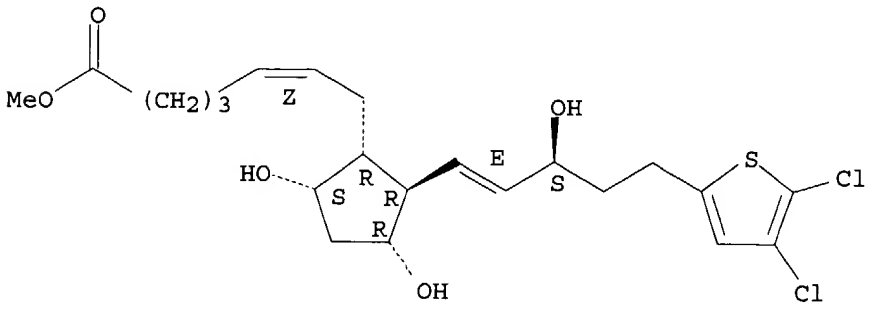
RN 225661-52-9 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(3,4-dibromo-5-methyl-2-thienyl)-3-methoxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



IT **225661-75-6 225661-77-8 225661-79-0**
225661-82-5 225661-84-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)
RN 225661-75-6 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4,5-dichloro-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

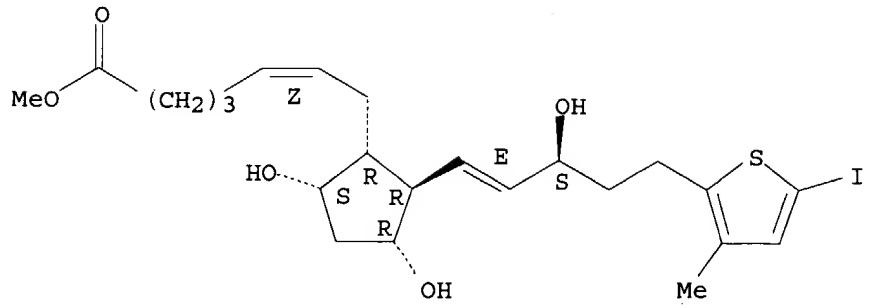
Relative stereochemistry.
Double bond geometry as shown.



RN 225661-77-8 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(5-iodo-3-methyl-2-thienyl)-1-pentenyl]cyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

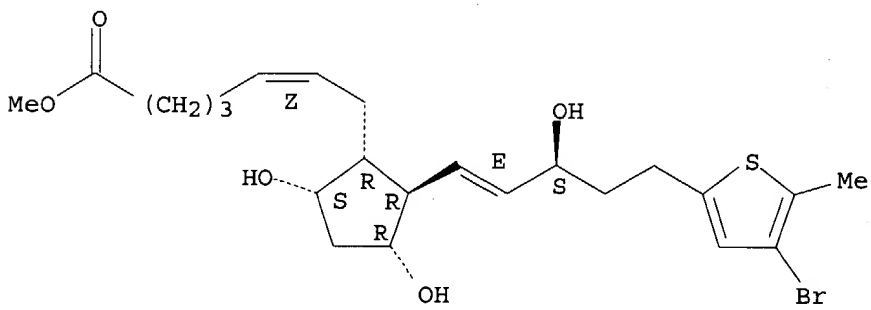
Relative stereochemistry.

Double bond geometry as shown.



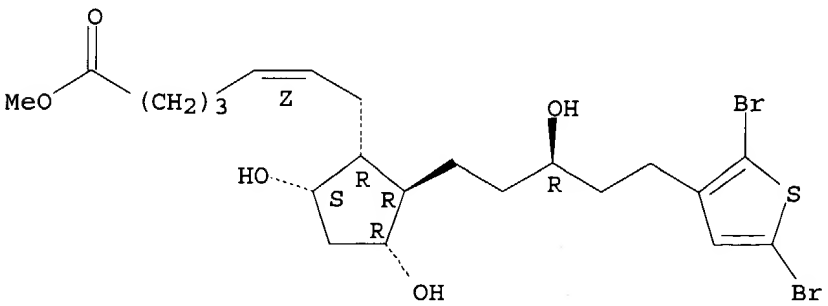
RN 225661-79-0 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(4-bromo-5-methyl-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 225661-82-5 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(3R)-5-(2,5-dibromo-3-thienyl)-3-hydroxypentyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

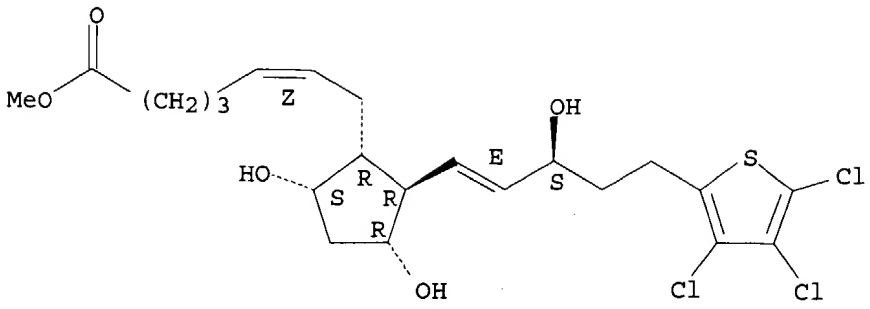
Relative stereochemistry.
Double bond geometry as shown.



RN 225661-84-7 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-(3,4,5-trichloro-2-thienyl)-1-pentenyl]cyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

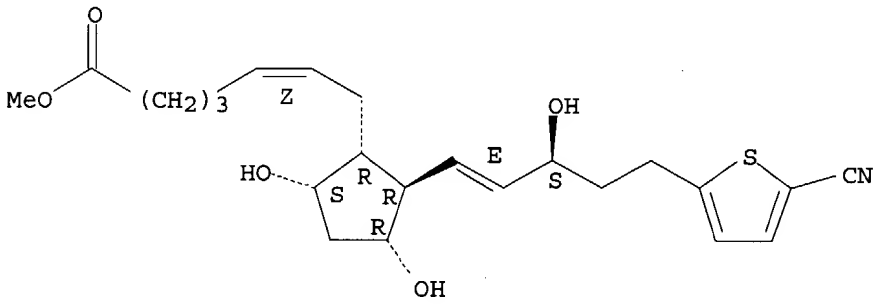


IT **225661-57-4P 225661-64-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclopentane heptan(ene)oic acid, 2-heteroarylalkenyl derivs. for use as **ocular hypertensive** agents)

RN 225661-57-4 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(1E,3S)-5-(5-cyano-2-thienyl)-3-hydroxy-1-pentenyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

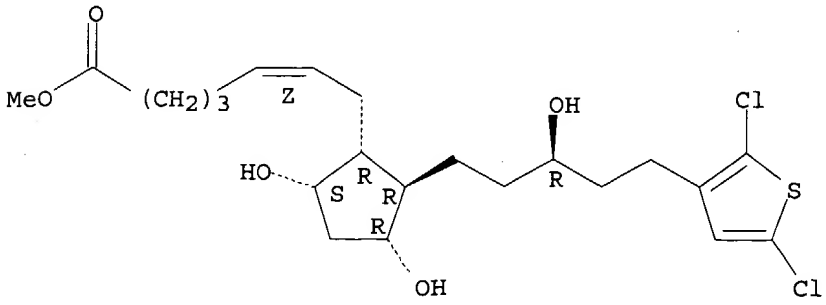
Relative stereochemistry.
Double bond geometry as shown.



RN 225661-64-3 HCAPLUS

CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-2-[(3R)-5-(2,5-dichloro-3-thienyl)-3-hydroxypentyl]-3,5-dihydroxycyclopentyl]-, methyl ester, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L113 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:64692 HCAPLUS
DN 130:119579
ED Entered STN: 01 Feb 1999
TI Prostaglandin derivatives devoid of side effects for the treatment of **glaucoma**
IN **Stjernschantz, Johan; Resul, Bahram; Lake, Staffan**
PA Pharmacia & Upjohn AB, Swed.
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-557
CC 1-1 (Pharmacology)
Section cross-reference(s): 26
FAN.CNT 1

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PI	WO 9902165	A1	19990121	WO 1998-SE1368	19980710	<--
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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	TR 200000008	T2	20000522	TR 2000-20000000819980710		<--
	EP 1014991	A1	20000705	EP 1998-934082	19980710	<--
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	BR 9815501	A	20010717	BR 1998-15501	19980710	<--
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	RU 2207858	C2	20030710	RU 2000-103224	19980710	<--
PRAI	SE 1997-2706	A	19970711	<--		
	WO 1998-SE1368	W	19980710	<--		

OS MARPAT 130:119579
AB A new method and compns. for the treatment of **glaucoma** and **ocular hypertension** are described. The method is based on the usage of **EP1** prostanoid receptor agonists which effectively reduce the **intraocular** pressure but have no, or reduced effect on iris pigmentation. The prostaglandin analog which is an **EP1** selective agonist is applied topically on the **eye.**
ST prostaglandin treatment **glaucoma**
IT **Prostanoid receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**EP1**; prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)
IT **Antiglaucoma agents**
Glaucoma (disease)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)
IT Prostaglandins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)

IT **4510-16-1P**, Pgf2β **38315-43-4P 219827-59-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)

IT **130225-92-2P 157019-93-7P 219827-55-1P**
219827-63-1P 219827-85-7P **219828-15-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)

IT 75-30-9, Isopropyl iodide 75-77-4, Trimethylsilyl chloride, reactions 456-41-7, 3-Fluorobenzyl bromide 688-73-3, Tributyltin hydride 1195-42-2, N-Isopropylcyclohexylamine 4202-14-6, Dimethyl 2-oxopropylphosphonate 14924-53-9, Ethyl cyclobutanecarboxylate 31752-99-5 61305-36-0 149862-39-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)

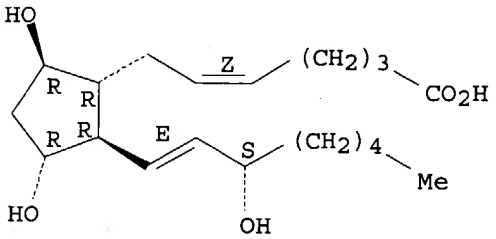
IT 38754-71-1P 39990-99-3P 62407-82-3P 62407-83-4P 62407-84-5P 63295-65-8P 219827-74-4P 219827-77-7P 219827-83-5P 219827-87-9P 219827-90-4P 219827-93-7P 219827-95-9P 219827-98-2P 219828-01-0P 219828-04-3P 219828-07-6P 219828-09-8P 219828-13-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alcon Laboratories, Inc; WO 9408585 A1 1994 HCAPLUS
(2) Bays, D; Natural product reports 1990, V7(5), P409 MEDLINE
(3) Kluender, H; US 4132738 A 1979 HCAPLUS
(4) Watabe, A; The Journal of Biological Chemistry 1993, V268(27), P20175 HCAPLUS
(5) Woodward, D; Journal of Lipid Mediators 1993, V6, P545 HCAPLUS

IT **4510-16-1P**, Pgf2β **38315-43-4P 219827-59-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)

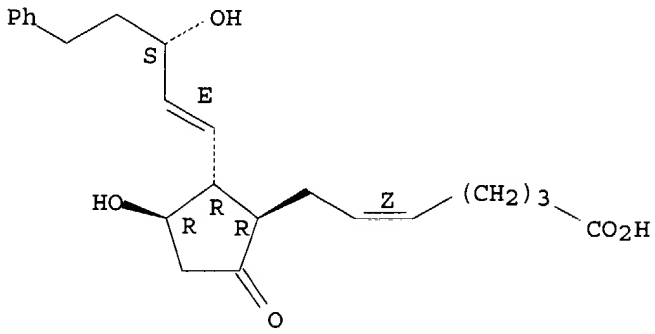
RN 4510-16-1 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9β,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



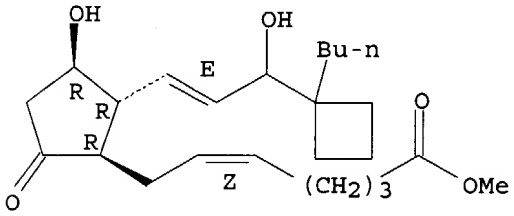
RN 38315-43-4 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



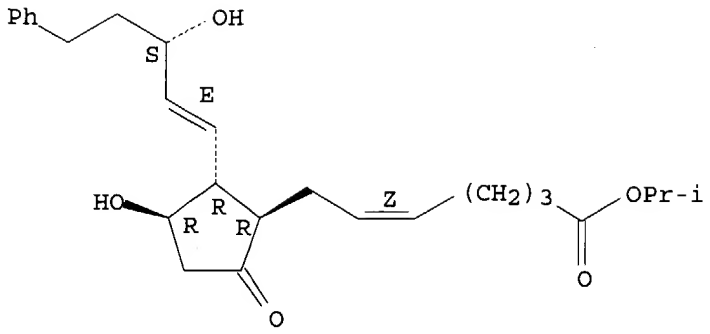
RN 219827-59-5 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(1E)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, methyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



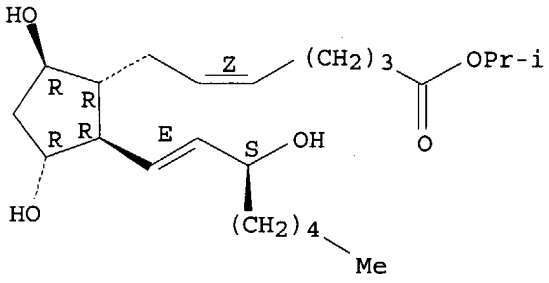
IT **130225-92-2P 157019-93-7P 219827-55-1P**
219827-63-1P 219828-15-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prostaglandin derivs. devoid of side effects for treatment of **glaucoma**)
RN 130225-92-2 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



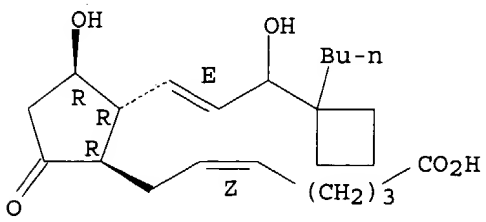
RN 157019-93-7 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9β,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



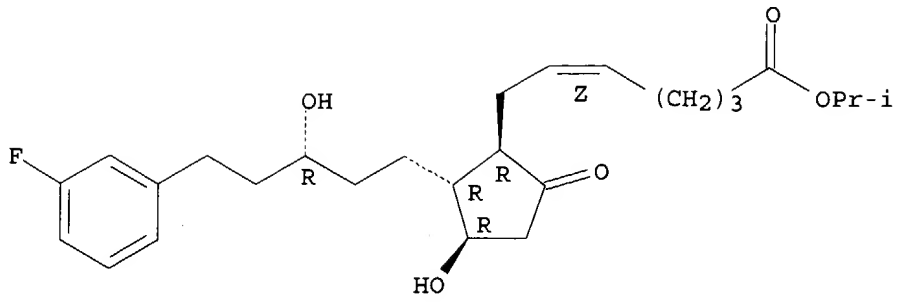
RN 219827-55-1 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(1E)-3-(1-butylcyclobutyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



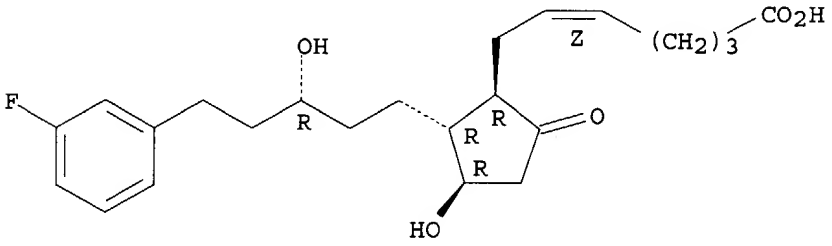
RN 219827-63-1 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(3R)-5-(3-fluorophenyl)-3-hydroxypentyl]-3-hydroxy-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 219828-15-6 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-2-[(3R)-5-(3-fluorophenyl)-3-hydroxypentyl]-3-hydroxy-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L113 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:272439 HCAPLUS
DN 126:339206
ED Entered STN: 28 Apr 1997
TI Prostaglandin effects on the contractility of bovine trabecular meshwork and ciliary muscle
AU Krauss, Achim H.-P.; Wiederholt, Michael; Strum, Annette; Woodward, David F.
CS Allergan, Inc., Irvine, CA, 92612, USA
SO Experimental Eye Research (**1997**), 64(3), 447-453
CODEN: EXERA6; ISSN: 0014-4835
PB Academic
DT Journal
LA English
CC 2-9 (Mammalian Hormones)
AB The **ocular hypotensive** activity of prostaglandins (PGs) has previously been demonstrated in various species including man. The underlying mechanism of action of prostanoids other than PGF2α remains contentious. Because the trabecular meshwork and ciliary muscle are believed to have a role in the regulation of aqueous humor outflow, the aim of this study was to identify the PG-receptor subtypes present in these tissues using receptor-selective agonists. Contractions of isolated strips of bovine trabecular meshwork and ciliary muscle were recorded isometrically in continuously perfused tissue chambers. Contractile activity of PGs was determined relative to a maximally effective concentration of carbachol (1 μM) as a standard agonist. The following prostanoids were employed: PGF2α, 17-Ph PGF2α (FP-receptor agonists), sulprostone (EP3 > **EP1**-agonist), AH13205 (EP2-agonist), 11-deoxy PGE1 (non-selective EP-agonist), and U-46619 (TP-agonist). The

thromboxane-mimetic U-46619 elicited a strong contraction of the trabecular meshwork with the highest concentration (1 μM) being almost twice as efficacious (186.6%) as the maximal carbachol concentration, whereas the effect on the ciliary muscle was small. The U-46619 induced trabecular meshwork contraction could be blocked with a potent and selective TP-receptor antagonist, 1 μM SQ29548, indicating the involvement of TP-receptors. The other PG-analogs studied had either no or a small but statistically significant effect. Thus, 17-Ph PGF2α (1 μM) weakly contracted the ciliary muscle (4.8%), sulprostone (1 μM) the trabecular meshwork (10.1%). 11-Deoxy PGE1 (1 μM) and AH13205 (10 μm) elicited relaxations in both tissues precontracted with carbachol (1 μM). The relaxant effects were more pronounced in trabecular meshwork (15.6% for 11-deoxy PGE1 and 21.4% for AH13205) than ciliary muscle (6.8 and 7.4% resp.). PGF2α did not elicit a significant response in either tissue. The studies suggest the existence of TP- and EP2-receptors in the bovine trabecular meshwork and potentially FP- and EP2-receptors in the ciliary muscle. In conclusion, thromboxane-mimetics and EP2-agonists have opposing activities on contractile elements in the meshwork and may modulate trabecular outflow in a functionally antagonistic manner. Prostanoid effects on ciliary muscle appear rather modest compared to parasympathomimetic drugs. It is conceivable that TP-agonists may substantially affect trabecular outflow.

ST prostaglandin eye ciliary muscle trabecular meshwork; PGF 2alpha eye

IT Eye
Eye
(ciliary muscle; prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Muscle
Muscle
(ciliary; prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Prostaglandins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Thromboxane receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT Eye
(trabecular meshwork; prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

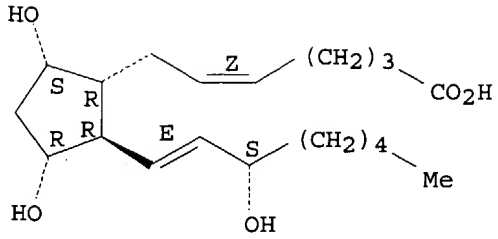
IT **551-11-1**, PGF2α **37786-00-8**, 11-Deoxy PGE1
55582-75-7, 17-Phenyl PGF2α 56985-40-1, U-46619
60325-46-4, Sulprostone 148436-63-9, AH13205
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

IT **551-11-1**, PGF2α **37786-00-8**, 11-Deoxy PGE1
55582-75-7, 17-Phenyl PGF2α
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prostaglandin effects on contractility of bovine trabecular meshwork and ciliary muscle)

RN 551-11-1 HCAPLUS

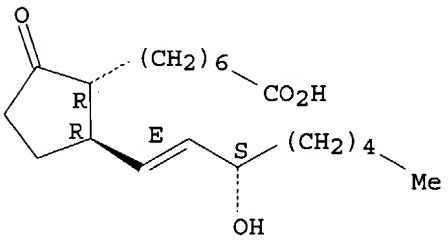
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



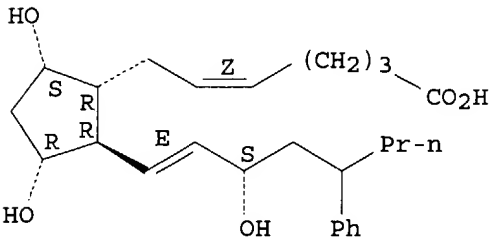
RN 37786-00-8 HCAPLUS
CN Prost-13-en-1-oic acid, 15-hydroxy-9-oxo-, (13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 55582-75-7 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-17-phenyl-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L113 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:215124 HCAPLUS
DN 122:232
ED Entered STN: 29 Nov 1994
TI Pharmacological characterization of prostaglandin-related **ocular hypotensive** agents
AU Goh, Yasumasa; Kishino, Junji
CS Shionogi Research Laboratories, Toyonaka, 561, Japan
SO Japanese Journal of Ophthalmology (**1994**), 38(3), 236-45
CODEN: JJOPA7; ISSN: 0021-5155
PB Japanese Journal of Ophthalmology
DT Journal
LA English
CC 1-2 (Pharmacology)

AB The agonistic activity of the prostaglandin (PG)-related **ocular hypotensive** agents, S-1033, UF-021 and PhXA34, to PG receptors was investigated by using in vitro tissue responses and binding of radio-labeled ligands to membranes. UF-021 and PhXA34, which are both 1-iso-Pr esterified forms, were examined mainly in a free acid form. The agonistic activity to PGD2 and PGI2 receptors, examined using inhibition of ADP-induced aggregation of guinea pig platelets, was negligible for all three compds. None showed substantial agonistic activity to TXA2 receptor, as determined from contractions of rat thorax aorta. PhXA34 showed significant **PGE2** agonistic activity. Among the three **PGE2** receptor subtypes, the agonistic activity to **EP1** and EP2 receptors was about 1/1000 and 1/2000 of **PGE2**, as determined from contraction of guinea pig longitudinal and circular ileum strips, resp. The other two compds. showed little agonistic activity (<1/100 000 of **PGE2**) to these receptors. The agonistic activity to PGF2α receptors, as determined from contraction of cat iris sphincter strips, was substantial for S-1033 and PhXA34, being 1/45 and 1/2 of PGF2α, resp., but weak for UF-021 (1/1600). To further investigate the affinity of the three compds. to **PGE2** and PGF2α receptors, inhibition of [3H]**PGE2**.alpha. binding was examined with membrane fractions of bovine adrenal medulla which possesses EP3 type **PGE2** receptors and bovine corpus luteum which has PGF2α receptors. The activity of PhXA34 for inhibiting [3H]**PGE2** binding was about 1/2000 of **PGE2**. S-1033 and UF-021 did not significantly inhibit [3H]**PGE2** binding within the range examined (<<1/2000 of **PGE2**). The activity to inhibit [3H]PGF2α binding was strong for PhXA34 (about the same as that of PGF2α), while the activity for S-1033 and UF-021 was about 1/34 and <1/280 of PGF2α, resp. These results indicate that the specificity to PGF2α receptor is the highest for S-1033 followed by PhXA34 although the activity to this receptor is stronger for the latter compound UF-021 has only a weak agonistic activity to PGF2α receptors.

ST S1033 UF021 PhXA34 prostaglandin thromboxane receptor; **eye hypotensive** S1033 UF021 PhXA34 prostaglandin

IT Prostaglandin receptors
Thromboxane receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ocular hypotensive** agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors)

IT **Glaucoma (disease)**
(**ocular hypotensive** agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors in relation to **glaucoma** treatment)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prostaglandin, **ocular hypotensive** agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors)

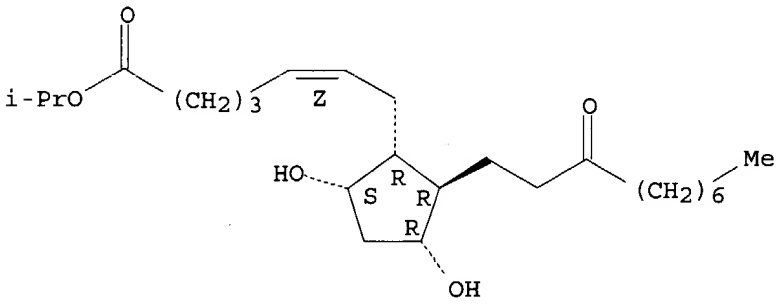
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thromboxane, **ocular hypotensive** agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors)

IT **120373-24-2**, UF-021 **138282-73-2**, S-1033
155551-81-8, PhXA34
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**ocular hypotensive** agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors)

IT **120373-24-2**, UF-021 **138282-73-2**, S-1033

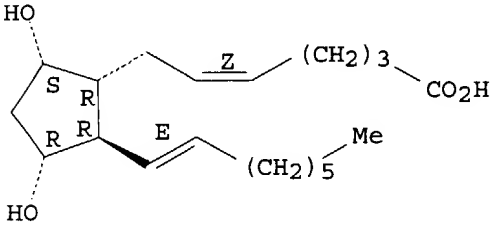
155551-81-8, PhXA34
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**ocular hypotensive** agents S-1033, UF-021, and PhXA34 agonistic activity to prostaglandin and thromboxane receptors)
RN 120373-24-2 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-(3-oxodecyl)cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

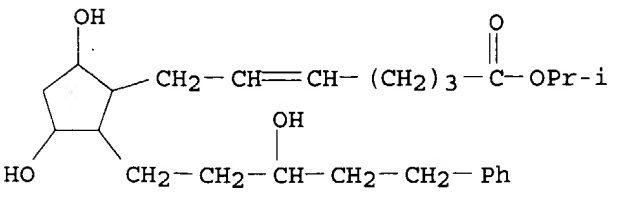


RN 138282-73-2 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11-dihydroxy-, monosodium salt, (5Z,9α,11α,13E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 155551-81-8 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenylpentyl)cyclopentyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

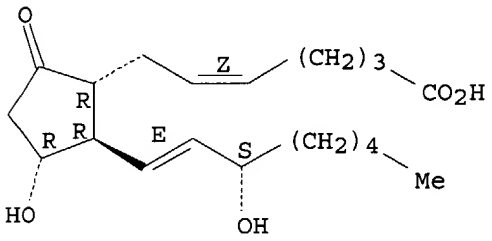


L113 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:290654 HCAPLUS

DN 120:290654
ED Entered STN: 11 Jun 1994
TI Studies on the **ocular hypotensive** effects of prostaglandin F2α prodrugs and receptor selective prostaglandin analogs
AU Woodward, David F.; Chan, M. F.; Burke, J. A.; Cheng-Bennett, A.; Chen, G.; Fairbairn, C. E.; Gac, T.; Garst, M. E.; Gluchowski, C.; et al.
CS Dep. Biochem., Allergan, Inc., Irvine, CA, USA
SO Journal of Ocular Pharmacology (**1994**), 10(1), 177-93
CODEN: JOPHER; ISSN: 8756-3320
DT Journal
LA English
CC 2-9 (Mammalian Hormones)
AB The use of natural prostaglandins (PG), such as PGD2, **PGE2**, PGF2α, and PGI2, for treating **glaucoma** is limited by their **ocular** side effects. One approach to achieve the required separation of **ocular hypotensive** activity from side effects is to employ ester prodrugs. From a novel series of 11- and 15-mono and 11,15-diacyl esters of PGF2α the authors identified prodrugs where PGF2α formation rates in the iris-ciliary body exceeded those in the conjunctiva, sclera, and corneal endothelium. Compared to PGF2α-1-iso-Pr ester the **ocular** tissue hydrolysis rates of the 11-monopivaloyl, the 11,15-dipivaloyl ester and the 1,11-lactone were ≤1000-fold less. Despite this large disparity in hydrolysis rates, the pivaloyl esters and the 1,11-lactone were potent **ocular hypotensives** in the authors' animal models. In studying prostaglandin analogs, the authors found that a diverse variety of prostanoid receptor selective agonists lowered **intraocular** pressure in dogs and/or monkeys. These included DP-, **EP1**-, EP2-, EP3-, and FP-receptor-selective compds. The receptor selectivity of these agonists was reexamd. by radioligand binding studies. Using radiolabeled **PGE2**, 17-Ph PGF2α, and sulprostone the authors were able to confirm the selectivity of the agonists currently used for receptor characterization directly by radioligand binding competition studies. It appears that multiple prostanoid receptor subtypes may be involved in regulating **intraocular** pressure.
ST prostanoid receptor subtype **intraocular** pressure; PGF 2alpha prodrug **ocular hypotensive**
IT Eye, metabolism
(conjunctiva, PGF2α formation from ester prodrugs in)
IT Eye, metabolism
(cornea, epithelium, PGF2α formation from ester prodrugs in)
IT Eye, metabolism
(cornea, stroma, PGF2α formation from ester prodrugs in)
IT **Eye**
(**intraocular** fluid, PGF2α prodrugs **hypotensive** effect on)
IT Eye, metabolism
(iris-ciliary body, PGF2α formation from ester prodrugs in)
IT Uterus, composition
(myometrium, prostanoid receptors of, prostanoid ligands interaction with)
IT Receptors
RL: BIOL (Biological study)
(prostaglandin, subtypes, of ocular tissues, intraocular pressure modulation by)
IT Prostaglandins
RL: BIOL (Biological study)
(receptors, subtypes, of ocular tissues, intraocular pressure modulation by)
IT **363-24-6**, **PGE2 40666-16-8**, Fluprostenol
41598-07-6, PGD2 **60972-43-2**, MB 28767 148436-63-9, AH 13205
RL: BIOL (Biological study)

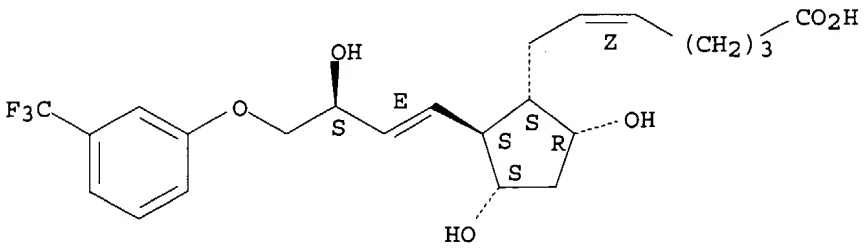
(myometrium prostanoid receptors interaction with)
IT **37786-00-8**, 11-Deoxy PGE1 **53764-90-2** 55314-48-2, PGF2α 1,9-lactone 55314-49-3, PGF2α 1,15-lactone **55582-75-7**, 17-Phenyl PGF2α 56985-40-1, U 46619 60325-46-4, Sulprostone 62410-84-8, PGF2α 1,11-lactone **134217-11-1 135273-39-1 135273-43-7** 137143-41-0 154887-01-1 154887-02-2
RL: PRP (Properties)
(**ocular hypotensive** effect of)
IT **551-11-1**, PGF2α
RL: BIOL (Biological study)
(prodrug hydrolysis to, in **eye**, **ocular hypotensive** effect of)
IT **363-24-6**, **PGE2** **40666-16-8**, Fluprostenol **60972-43-2**, MB 28767
RL: BIOL (Biological study)
(myometrium prostanoid receptors interaction with)
RN 363-24-6 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



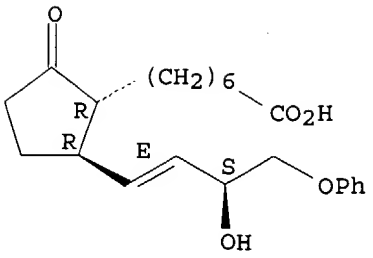
RN 40666-16-8 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-[3-(trifluoromethyl)phenoxy]-1-butenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



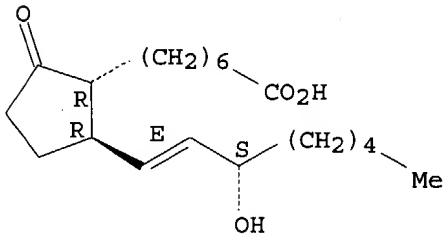
RN 60972-43-2 HCAPLUS
CN Cyclopentaneheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]-5-oxo-, (1S,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



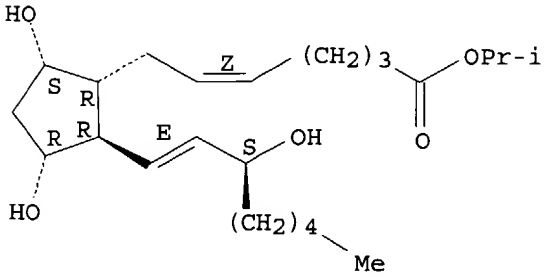
IT **37786-00-8**, 11-Deoxy PGE1 **53764-90-2 55582-75-7**
, 17-Phenyl PGF2α **134217-11-1 135273-39-1**
135273-43-7
RL: PRP (Properties)
(**ocular hypotensive** effect of)
RN 37786-00-8 HCAPLUS
CN Prost-13-en-1-oic acid, 15-hydroxy-9-oxo-, (13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



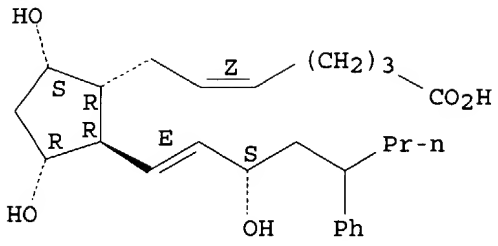
RN 53764-90-2 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



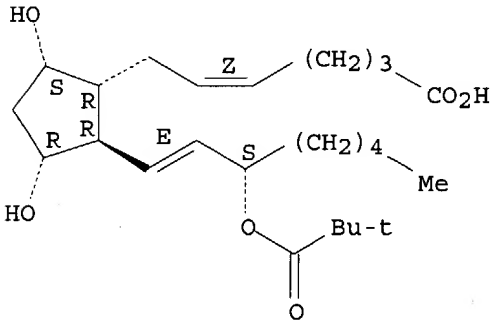
RN 55582-75-7 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-17-phenyl-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



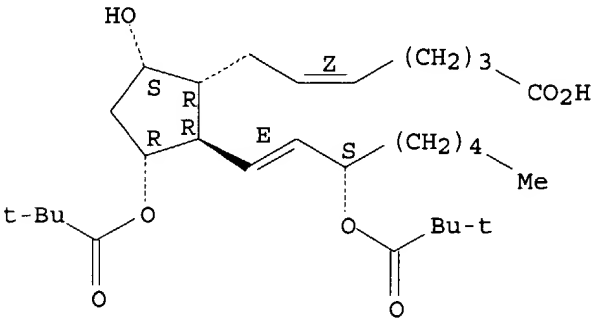
RN 134217-11-1 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 15-(2,2-dimethyl-1-oxopropoxy)-9,11-dihydroxy-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



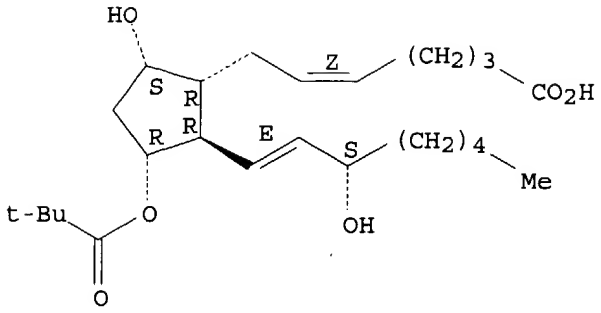
RN 135273-39-1 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-bis(2,2-dimethyl-1-oxopropoxy)-9-hydroxy-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



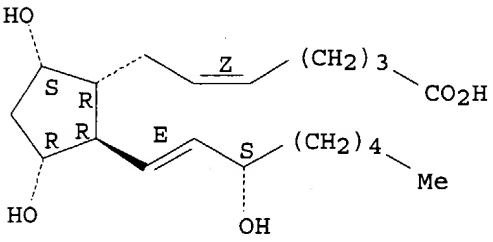
RN 135273-43-7 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 11-(2,2-dimethyl-1-oxopropoxy)-9,15-dihydroxy-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **551-11-1**, PGF2α
RL: BIOL (Biological study)
(prodrug hydrolysis to, in **eye**, **ocular** **hypotensive** effect of)
RN 551-11-1 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L113 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:596454 HCAPLUS
DN 119:196454
ED Entered STN: 13 Nov 1993
TI Intraocular pressure effects of selective prostanoid receptor agonists involve different receptor subtypes according to radioligand binding studies
AU Woodward, David F.; Lawrence, Ruth A.; Fairbairn, Casey E.; Shan, Tanwir; Williams, Linda S.
CS Dep. Biol. Sci., Allergan, Inc., Irvine, CA, 92713-9534, USA
SO Journal of Lipid Mediators (**1993**), 6(1-3), 545-53
CODEN: JLMEEG; ISSN: 0921-8319
DT Journal
LA English
CC 2-9 (Mammalian Hormones)
AB The receptors involved in the **ocular** **hypotensive** activity **PGE2** and PGF2α in dogs and monkeys were investigated by examining the effects of putative receptor selective agonists on **intraocular** pressure. A diverse variety of receptor selective agonists lowered **intraocular** pressure in these species. Thus, FP-receptor agonists (17-Ph PGF2α, fluprostenol), agonists with potent activity at the EP3 receptor (MB 28767, sulprostone) and a prostanoid with activity at the EP2 receptor (11-deoxy PGE1) were all potent **ocular** **hypotensives** when administered as a single dose to dogs and monkeys or b.i.d. for 5 days in monkeys. These findings were regarded as surprising and prompted re-exam. of some aspects

of the current classification for prostanoid receptors. At present certain receptor subtypes, notably EP2, EP3, and FP receptors, are defined only according to potency rank order for agonists. In these studies, the authors employed radioligand binding studies to determine the degree of competition between prostanoid agonists claimed to be selective on the basis of functional assays. Competition studies with the myometrial plasma membrane prepared from the rat uterus were consistent with the presence of an EP3 receptor. Thus, EP3-receptor agonists (MB 28767 and sulprostone) potently inhibited **PGE2** and sulprostone binding, whereas FP agonists (17-Ph PGF2α, fluprostenol), a DP agonist (BW 245C), an **EP1** antagonist (AH 6809), and EP2 agonist (AH 13205) and TP-receptor ligands (BM 13505, I-BOP) afforded little or no inhibition. Radioligand binding studies in plasma membrane prepns. from the rat colon with 17-Ph [3H]PGF2α were consistent with the presence of an FP-receptor. 17-Ph [3H]PGF2α was potently displaced by PGF2α, whereas only very weak competition at the receptor site was afforded by EP3 agonists (MB 28767, sulprostone). The results are consistent with the existence of EP3 and FP receptors as distinct entities. The findings also imply that the decrease in **intraocular** pressure produced by FP and EP3 agonists results from stimulation of two independent subpopulations of prostanoid receptors.

ST eye intraocular pressure prostaglandin receptor agonist

IT Eye
(intraocular pressure of, prostaglandin receptor subtypes in regulation of)

IT Prostaglandins
RL: BIOL (Biological study)
(EP3 receptors, in eye intraocular pressure regulation)

IT Prostaglandins
RL: BIOL (Biological study)
(FP receptors, in eye intraocular pressure regulation)

IT Receptors
RL: BIOL (Biological study)
(prostaglandin EP3, in eye intraocular pressure regulation)

IT Receptors
RL: BIOL (Biological study)
(prostaglandin FP, in eye intraocular pressure regulation)

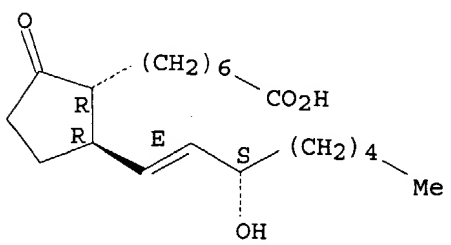
IT **37786-00-8**, 11-Deoxy PGE1 **40666-16-8**, Fluprostenol
55582-75-7, 17-Phenyl PGF2α 60325-46-4, Sulprostone
60972-43-2, MB 28767
RL: BIOL (Biological study)
(eye intraocular pressure decrease by)

IT **37786-00-8**, 11-Deoxy PGE1 **40666-16-8**, Fluprostenol
55582-75-7, 17-Phenyl PGF2α **60972-43-2**, MB 28767
RL: BIOL (Biological study)
(eye intraocular pressure decrease by)

RN 37786-00-8 HCAPLUS

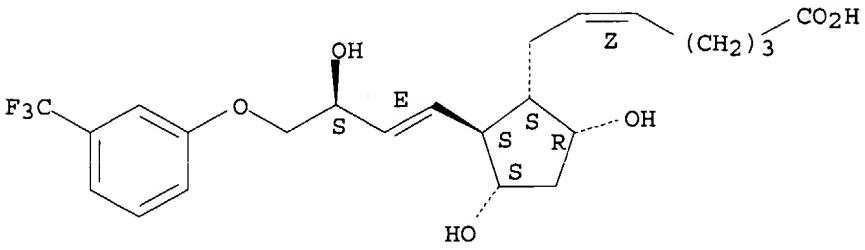
CN Prost-13-en-1-oic acid, 15-hydroxy-9-oxo-, (13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



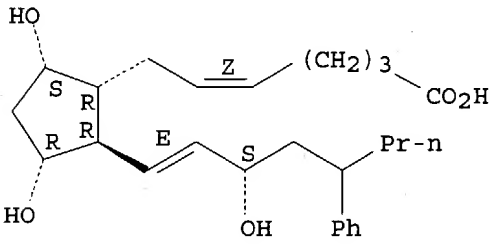
RN 40666-16-8 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-[3-(trifluoromethyl)phenoxy]-1-butenyl]cyclopentyl]-, (5Z)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



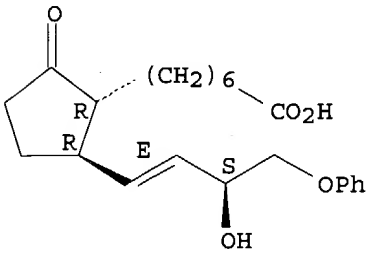
RN 55582-75-7 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-17-phenyl-, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 60972-43-2 HCAPLUS
CN Cyclopentaneheptanoic acid, 2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]-5-oxo-, (1S,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L113 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1990:605515** HCAPLUS
DN **113:205515**
ED Entered STN: 08 Dec 1990
TI Preparation and use of prostaglandin derivatives for the treatment of **glaucoma** or **ocular hypertension**

	JP 08109132	A2	19960430	JP 1995-241200	19950920	<--
	JP 2955213	B2	19991004			
	US 6030999	A	20000229	US 1999-307814	19990510	<--
	US 6187813	B1	20010213	US 1999-307813	19990510	<--
	US 6429226	B1	20020806	US 2000-562447	20000501	<--
	US 2001014693	A1	20010816	US 2001-781896	20010212	<--
	US 6417230	B2	20020709			
	US 2002173525	A1	20021121	US 2002-106228	20020327	<--
	US 2003166729	A1	20030904	US 2002-288732	20021105	<--
	US 2003181493	A1	20030925	US 2002-330846	20021227	<--
PRAI	SE 1988-3110	A	19880906	<--		
	SE 1988-3855	A	19881028	<--		
	EP 1989-850294	A	19890906	<--		
	EP 1993-109514	A3	19890906	<--		
	EP 2002-9256	A3	19890906	<--		
	EP 2003-516	A3	19890906	<--		
	JP 1995-241200	A3	19890906	<--		
	WO 1989-SE475	A	19890906	<--		
	US 1990-469442	B1	19900410	<--		
	US 1991-740371	B1	19910724	<--		
	US 1992-986943	A3	19921208	<--		
	US 1992-988389	A1	19921208	<--		
	US 1995-461341	A1	19950605	<--		
	US 1999-307813	A1	19990510			
	US 2001-781896	A1	20010212			
	US 2002-106228	A1	20020327			

OS MARPAT 113:205515

AB Ophthalmol. compns. for topical treatment of **glaucoma** or **ocular hypertension** comprise, in an ophthalmol. compatible carrier, an effective amount of a derivative of PGA, PGB, PGD, PGE, or PGF having an ω-chain C13BC14DR2 [B is a single, double, or triple bond between C13 and C14; D = (un)substituted C1-10 chain optionally interrupted by O, S, or N; R2 = (un)substituted ring]. Thus, crude 15-(R,S)-17-phenyl-18,19,20-trinor-PGF2α (preparation given) was esterified and purified by column chromatog. to give 15-(R)-17-phenyl-18,19,20-trinor-PGF2α isopropyl ester (I) in 46% yield. I (10 μg) reduced **intraocular** pressure in healthy human volunteers to 11.2 mm Hg 8 h after administration (control = 15.1 mm Hg at 8 h). I and other prepared prostaglandin derivs. all significantly reduced **intraocular** pressure without significant irritating effect (**ocular** discomfort); 2 of the derivs. caused little, if any, conjunctival/episcleral hyperemia in man.

ST prostaglandin deriv **glaucoma** treatment; PGF deriv **glaucoma** treatment

IT **Glaucoma (disease)**
(treatment of, with prostaglandin derivs.)

IT Prostaglandins
RL: PREP (Preparation)
(A, 18,19,20-trinor-, 13,14-dihydro-17-Ph, alkyl esters, preparation of, for **glaucoma** treatment)

IT Prostaglandins
RL: PREP (Preparation)
(A, 18,19,20-trinor-, 15-dehydro-17-Ph, alkyl esters, preparation of, for **glaucoma** treatment)

IT Prostaglandins
RL: PREP (Preparation)
(E, 18,19,20-trinor-, 13,14-dihydro-17-Ph, alkyl esters, preparation of, for **glaucoma** treatment)

IT Prostaglandins
RL: PREP (Preparation)
(E, 18,19,20-trinor-, 15-dehydro-17-Ph, alkyl esters, preparation of, for **glaucoma** treatment)

IT Prostaglandins

RL: PREP (Preparation)
(F, 18,19,20-trinor-, 13,14-dihydro-17-Ph, alkyl esters, preparation of, for **glaucoma** treatment)

IT Prostaglandins
RL: PREP (Preparation)
(F, 18,19,20-trinor-, 15-dehydro-17-Ph, alkyl esters, preparation of, for **glaucoma** treatment)

IT **38315-43-4**, 17-Phenyl-18,19,20-trinor **PGE2**
38315-48-9 38344-08-0 51705-19-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, in preparation of prostaglandin derivative for **glaucoma** treatment)

IT 38754-71-1P 41639-72-9P 52343-56-3P 88257-37-8P 130209-85-7P
130273-88-0P 130273-89-1P **130273-90-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in prostaglandin derivative preparation for **glaucoma** treatment)

IT **130209-75-5P 130209-76-6P 130209-77-7P**
130209-78-8P 130209-79-9P **130209-81-3P**
130209-82-4P 130209-83-5P 130209-84-6P
130225-92-2P 130273-87-9P
RL: PREP (Preparation)
(preparation of, for **glaucoma** treatment)

IT 31752-99-5 130209-80-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of prostaglandin derivative for **glaucoma** treatment)

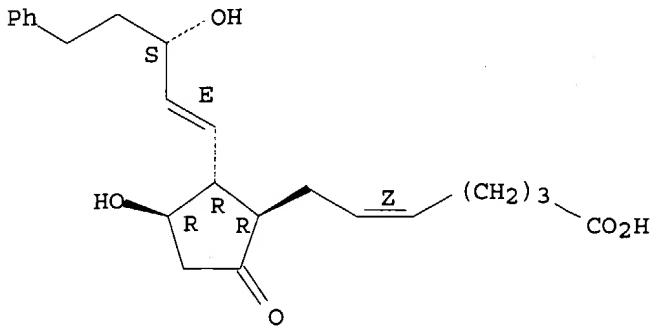
IT 41162-19-0, Dimethyl-2-oxo-4-phenylbutyl phosphonate 52344-42-0
61263-11-4, Dimethyl-2-oxo-6-phenyl-hexylphosphonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prostaglandin derivative preparation for **glaucoma** treatment)

IT 75-30-9, Isopropyl iodide 41029-44-1, Isopropyl triflate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with prostaglandin, in prostaglandin derivative preparation for **glaucoma** treatment)

IT **38315-43-4**, 17-Phenyl-18,19,20-trinor **PGE2**
38315-48-9 38344-08-0 51705-19-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, in preparation of prostaglandin derivative for **glaucoma** treatment)

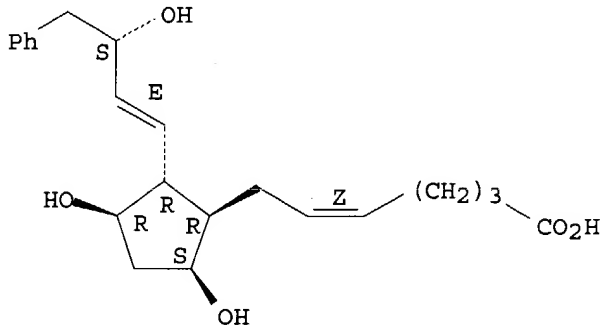
RN 38315-43-4 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



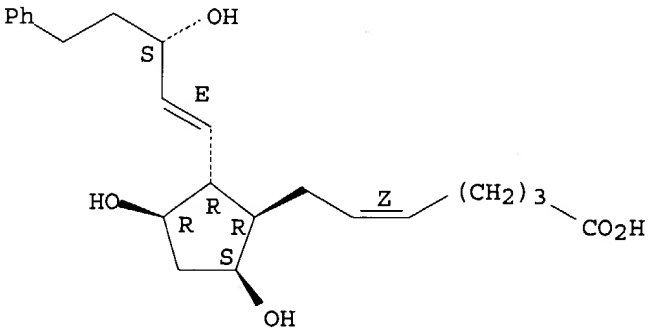
RN 38315-48-9 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-4-phenyl-1-butenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



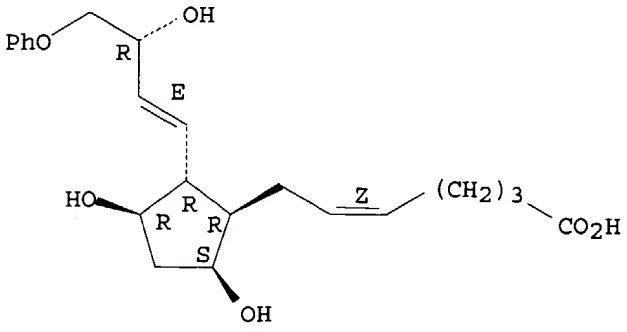
RN 38344-08-0 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

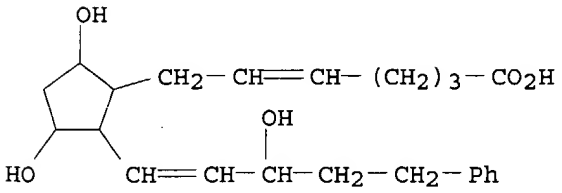


RN 51705-19-2 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-phenoxy-1-butenyl]cyclopentyl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

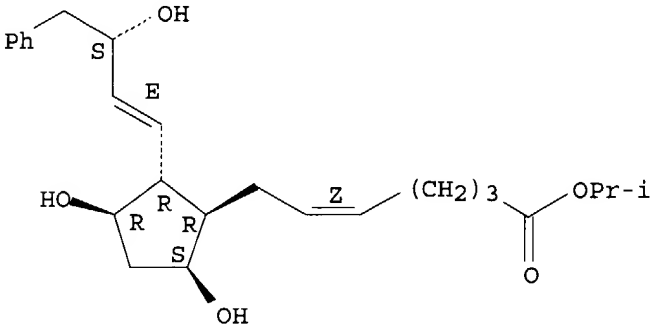


IT **130273-90-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in prostaglandin derivative preparation for **glaucoma** treatment)
RN 130273-90-4 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenyl-1-pentenyl)cyclopentyl]- (9CI) (CA INDEX NAME)



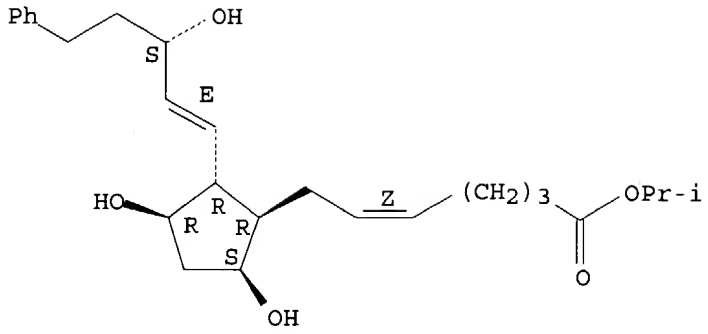
IT **130209-75-5P 130209-76-6P 130209-77-7P**
130209-78-8P 130209-81-3P 130209-82-4P
130209-83-5P 130209-84-6P 130225-92-2P
130273-87-9P
RL: PREP (Preparation)
(preparation of, for **glaucoma** treatment)
RN 130209-75-5 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-4-phenyl-1-butenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1α(Z),2β(1E,3S*),3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



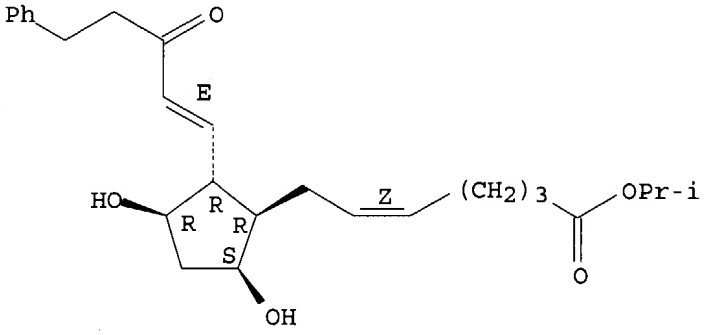
RN 130209-76-6 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



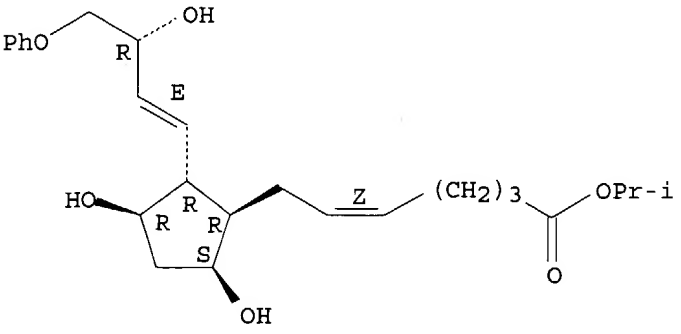
RN 130209-77-7 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E)-3-oxo-5-phenyl-1-pentenyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



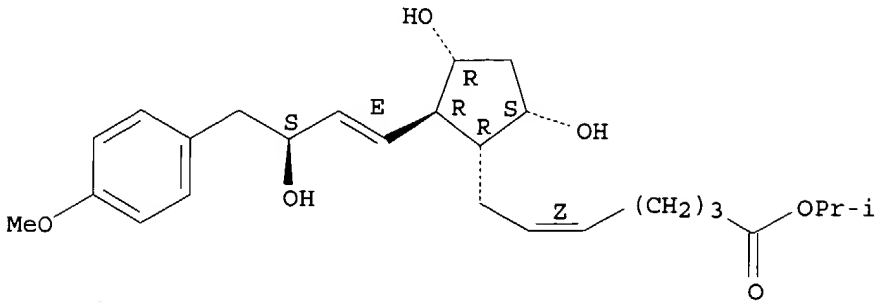
RN 130209-78-8 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-4-phenoxy-1-butenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1α(Z),2β(1E,3R*),3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



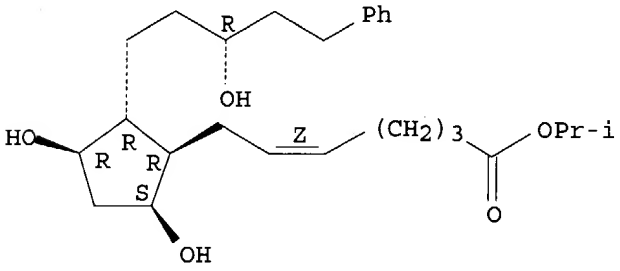
RN 130209-81-3 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-[3-hydroxy-4-(4-methoxyphenyl)-1-butenyl]cyclopentyl]-, 1-methylethyl ester, [1R-[1α(Z),2β(1E,3S*),3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



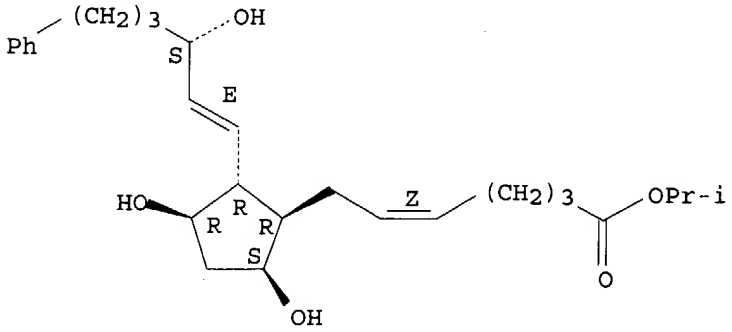
RN 130209-82-4 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



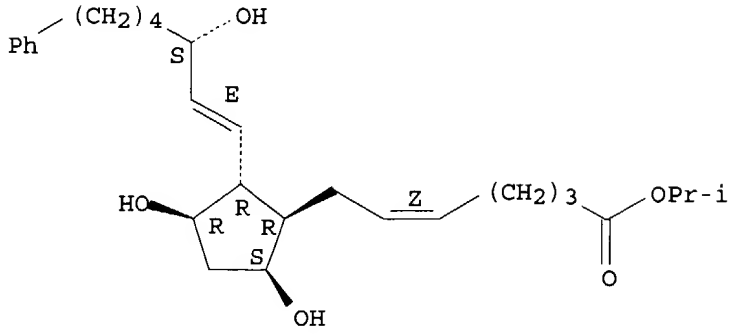
RN 130209-83-5 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-6-phenyl-1-hexenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1α(Z),2β(1E,3S*),3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



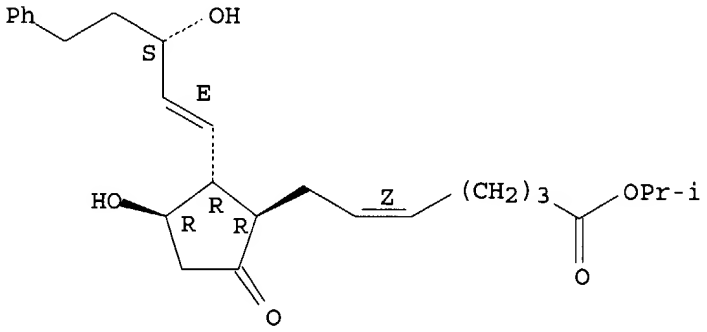
RN 130209-84-6 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-7-phenyl-1-heptenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1α(Z),2β(1E,3S*),3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



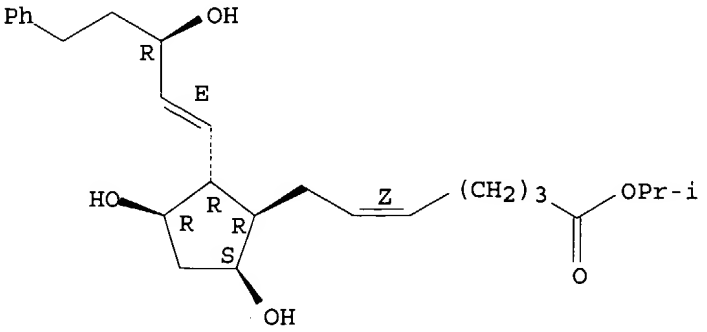
RN 130225-92-2 HCAPLUS
CN 5-Heptenoic acid, 7-[(1R,2R,3R)-3-hydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]-5-oxocyclopentyl]-, 1-methylethyl ester, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



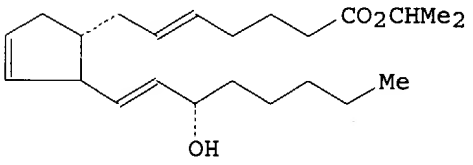
RN 130273-87-9 HCAPLUS
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-5-phenyl-1-pentenyl)cyclopentyl]-, 1-methylethyl ester, [1R-[1α(Z),2β(1E,3R*),3α,5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L113 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

AN **1990:401022** HCAPLUS
DN **113:1022**
ED Entered STN: 06 Jul 1990
TI Eicosanoids as a new class of **ocular hypotensive** agents. 3. Prostaglandin A2-1-isopropyl ester is the most potent reported **hypotensive** agent on feline **eyes**
AU Bito, Laszlo Z.; Miranda, Olivia C.; Tendler, Michael R.; **Resul, Bahram**
CS Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SO Experimental Eye Research (**1990**), 50(4), 419-28
CODEN: EXERA6; ISSN: 0014-4835
DT Journal
LA English
CC 2-9 (Mammalian Hormones)
GI



I

AB **Intraocular** pressure reduction can be achieved in normotensive cat **eyes** with the use of even lower doses of PGA2-1-iso-Pr ester (PGA2-IE) (I) than with PGA2, PGF2α-1-iso-Pr ester (PGF2α-IE), or any other known **ocular hypotensive** agent. Furthermore, single applications of 0.5 μg of I maintain IOP redns. for ≤24 h. This **hypotensive** effect is enhanced during the first 3-5 days of daily treatment. IOP redns. were maintained for several months as long as I was applied daily or at least once every 48 h. None of the cats manifested signs of discomfort in response to treatment with doses ranging 0.10 - 1.25 μg I. Moreover, the extent of anterior chamber flare was less than that typically observed after the topical application of **hypotensive** doses of **PGE2**, PGD2, PGF2α, or the esters or tromethamine salt of PGF2α. Although it is possible that the human **eye** would respond differently to prostaglandins of the A type, I or other esters of derived PGs of the A type, and probably the B type, may offer therapeutic advantages over the PGF2α tromethamine salt and PGF2α-IE, which have been shown to exert **hypotensive** effects on normal and **glaucomatous** human **eyes.**

ST prostaglandin A ester **ocular hypotensive**; PGA2 isopropyl ester **intraocular** pressure; **glaucoma** PGA2 isopropyl ester

IT Eye
(intraocular pressure of, PGA2 iso-Pr ester decrease of)

IT **Glaucoma (disease)**
(treatment of, with PGA2 iso-Pr ester)

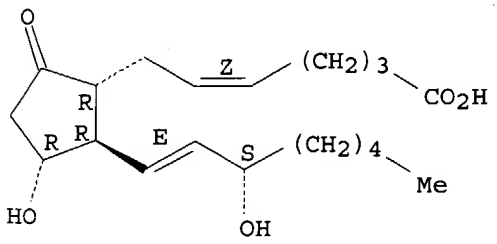
IT Prostaglandins
RL: BIOL (Biological study)
(A, esters, eye intraocular pressure decrease by)

IT **363-24-6**, **PGE2** 13345-50-1, PGA2 13367-85-6, PGB2 **38562-01-5**, PGF2α-THAM **53764-90-2** 114084-85-4
RL: BIOL (Biological study)
(eye intraocular pressure decrease by)

IT **363-24-6**, **PGE2** **38562-01-5**, PGF2α-THAM **53764-90-2**
RL: BIOL (Biological study)
(eye intraocular pressure decrease by)

RN 363-24-6 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

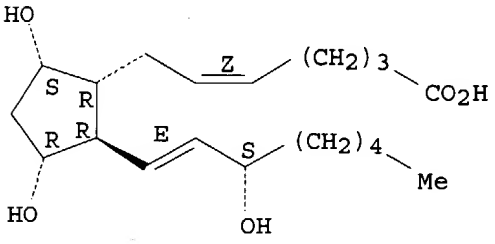


RN 38562-01-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,9α,11α,13E,15S)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

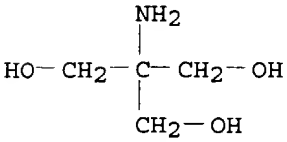
CRN 551-11-1
CMF C20 H34 O5

Absolute stereochemistry.
Double bond geometry as shown.



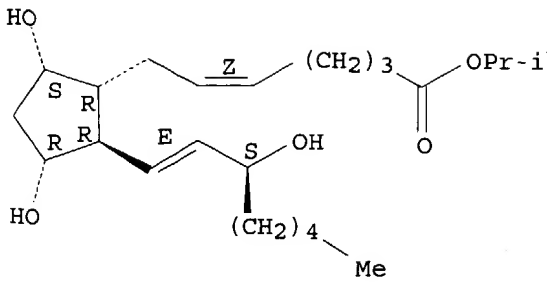
CM 2

CRN 77-86-1
CMF C4 H11 N O3



RN 53764-90-2 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, 1-methylethyl ester, (5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.


HO
Z
(CH2)3
OPr-i
S
R
R
R
E
S
OH
O
HO
(CH2)4
Me

=>